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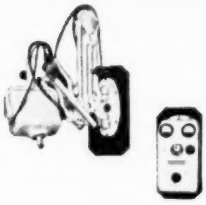

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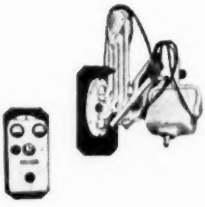

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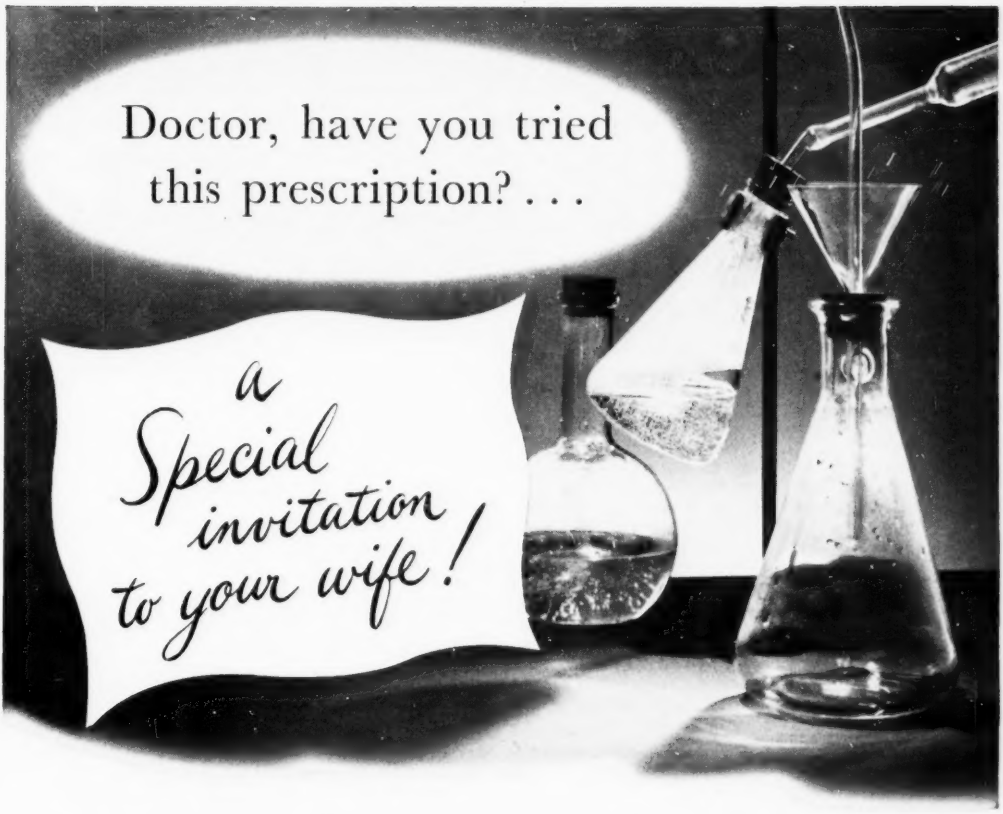

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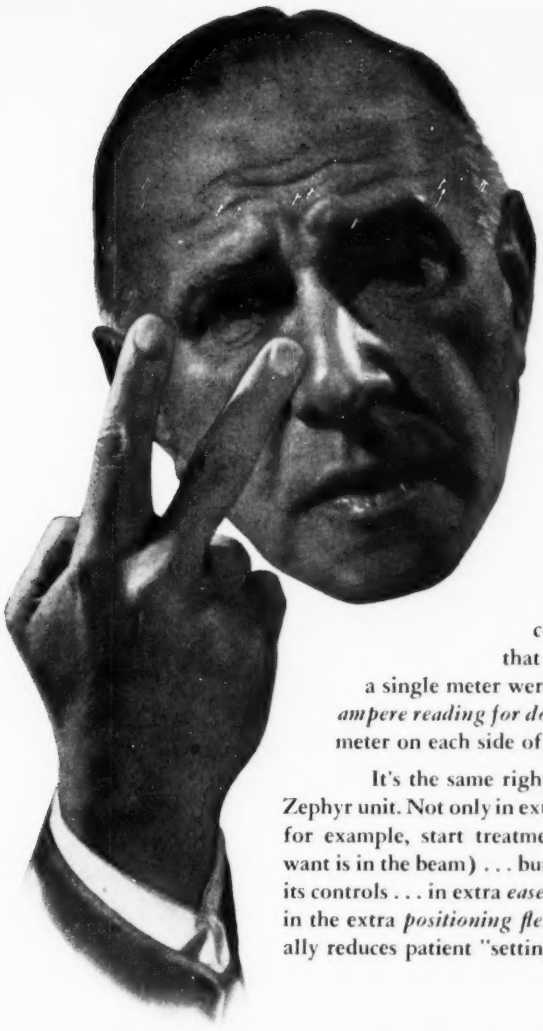

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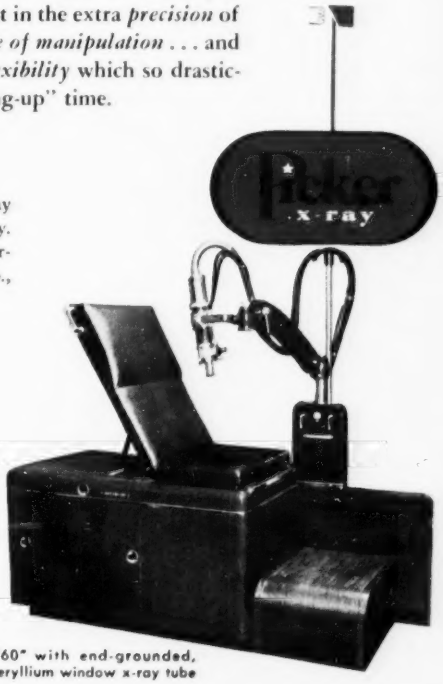

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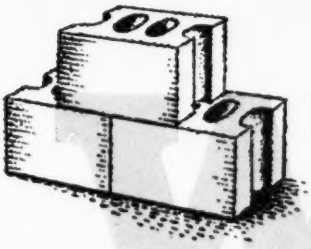

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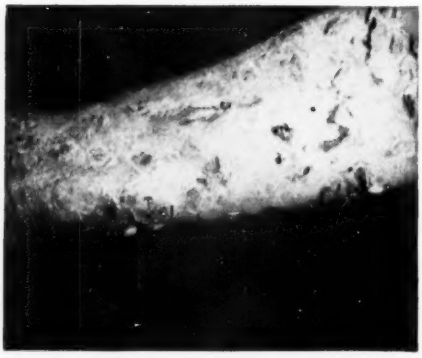

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Archives of Dermatology and Syphilology

VOLUME 67 MARCH 1953 NUMBER 3

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SYSTEMIC DISTURBANCES IN RECALCITRANT TRICHOPHYTON RUBRUM (PURPUREUM) INFECTIONS

Studies and Short Report on Therapeutic Experiments

STEPHEN ROTHMAN, M.D.
CHICAGO

MATERIAL

THE MATERIAL presented here consists of 20 adult patients suffering from therapy-resistant Trichophyton rubrum (purpureum) infections of the palms, soles, toenails, and fingernails observed within the last three years at the University of Chicago Clinics.

The palmar and plantar manifestations included superficial circinate and annular scaling lesions reminiscent of keratolysis exfoliativa, punctate hyperkeratotic lesions, and diffuse hyperkeratotic and callous lesions.

The infected nails showed the well-known disintegration of the plates starting at the distal end but eventually involving the whole plate. In some cases an unusually hard subungual rippled hyperkeratosis was present. Vesicle formation and interdigital maceration were either not seen at all, or if they were present they responded readily to local application of fungistatic agents. In some cases the hyperkeratosis extended to the interdigital spaces, and such hyperkeratoses were as resistant as those on palms and soles.

No other areas but palms, soles, and nails were permanently involved in these cases. Lesions appearing elsewhere cleared up under routine fungistatic management in a short time and did not recur. In contrast, the lesions of soles and palms and the onychomycosis were absolutely therapy resistant. It is controversial whether all forms of T. rubrum infections are therapy-resistant. Lewis, Montgomery, and Hopper [1] found hyperkeratotic lesions caused by T. rubrum to be unusually resistant, whereas Weidman and Glass [2] reported that in tinea pedis hyperkeratotic lesions due to Trichophyton mentagrophytes were at least as resistant as those due to T. rubrum. The duration of the disease was from 2 to 28 years and averaged 8 years. Prior to admission to our clinic all patients had seen competent dermatologists, and in all of them a great number of fungistatic agents had been tried. Nevertheless, in this series of patients on admission the organisms could be demonstrated microscopically and culturally with great ease in practically all scraped-off particles of the affected horny layer and from all nail fragments.

This work was supported in part by a grant from Hoffmann-La Roche, Inc.

From the Section of Dermatology, Department of Medicine, University of Chicago.

Read at the Seventy-Second Annual Meeting of the American Dermatological Association, Colorado Springs, Colo., April 24, 1952.

1. Lewis, G. M.; Montgomery, R. M., and Hopper, M. E.: Cutaneous Manifestations of Trichophyton Purpureum (Bang), Arch. Dermat. & Syph. **37**:823, 1938.

2. Weidman, F. D., and Glass, F.: Dermatophytosis and Other Forms of Intertriginous Dermatitis of the Feet, Arch. Dermat. & Syph. **53**:213, 1946.

REGIONAL SUSCEPTIBILITY

As is often the case in onychomycosis, it was conspicuous that some of the nail plates on the affected hand or foot remained free of infection even after the onychomycosis on other nails had persisted for years or decades. Even more conspicuous was the unilateral involvement of one palm for many years with complete freedom of the other palm. There were 13 patients with palmar involvement, which in 6 was unilateral. In five of the latter patients the right palm was involved; in only one patient was there left palmar involvement. All six patients were right-handed. The great prevalence of right palm involvement suggested that the greater use of the right hand might have been significant in its greater susceptibility. Possibly this has something to do with increased sweat secretion. Kuno [3] showed that on palms and soles sweat is most abundant in those areas where pressure is habitual. The affinity of T. rubrum to palmar skin in itself is remarkable as being in sharp contrast to the extreme rarity of palmar involvement in T. mentagrophytes infections.

In any case, it appears that there are hitherto unexplained regional or local susceptibility factors operating in T. rubrum infection.

INDIVIDUAL SUSCEPTIBILITY

We could not ascertain a single instance in which the infection would have been transferred from one person to another in the family, to fellow workers, or to the medical and laboratory personnel. We could not find data in the literature either about direct transfer from person to person, a remarkable negative finding because localization on palms and fingernails offers plenty of opportunity for such transfer. Apparently T. rubrum infection of the hands and fingernails is not contagious at all or its contagiosity is low-grade. This indicates that possibly some individual predisposition is required for the take of this infection.

In widespread T. rubrum infections involving face, trunk, extremities, and nails, ichthyosis or other ichthyosiform congenital anomalies with decreased sweat secretion were assumed to be such a predisposing factor,[4] in diametric opposition to what the preferential involvement of the right palm would indicate. Widespread infections in ichthyotic persons were reported by Lane [5] and by Swartz and Conant,[6] and in a person with a hyperkeratotic "nevoid anomaly of the skin" by Baer and Muskatblit.[4] The last two authors have demonstrated quantitatively the decreased sweating ability of their patient.

However, in our cases with exclusive hand and foot involvement, ichthyosiform anomalies were not present. Regarding local sweating ability, about half the patients had conspicuously dry palms, also in uninvolved sites, but the other half had either normal or increased sweating ability on their palms.

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3. Kuno, Y.: The Physiology of Human Perspiration, London, J. & A. Churchill, Ltd., 1934.

4. Baer, R. L., and Muskatblit, E.: Extensive Trichophyton Purpureum Infection with Nevoid Anomaly of the Skin, Arch. Dermat. & Syph. **56**:834, 1947.

5. Lane, C. G.: Tinea Corporis (Trichophyton Purpureum): Moniliasis of Feet; Ichthyosis, Arch. Dermat. & Syph. **40**:119, 1939.

6. Swartz, J. H., and Conant, N. F.: Extensive Lichenified Eruption Caused by Trichophyton Rubrum, Arch. Dermat. & Syph. **42**:614, 1940.

ANOMALY OF THE ORAL GLUCOSE TOLERANCE TEST

The opportunity to search for an entirely different constitutional factor arose six years ago when I observed a case of widespread T. rubrum infection comparable to the cases reported by Lewis, Montgomery, and Hopper,[1] Muskatblit,[7] Ayres,[8] and Swartz and Conant.[6]

CASE 1.—A 26-year-old automobile salesman was admitted to the University of Chicago Clinics on May 11, 1946. He had lesions on the neck, trunk, and extremities of two years' duration. In addition to tinea circinata-like lesions, there were papules, eczematiform crusted but figurated lesions, and lichenified lesions simulating dry neurodermatitis. Microscopically all lesions yielded fungi abundantly, and T. rubrum grew out on cultures from all sites.

The patient was obese, pale pasty, slow in all his reactions, and sensitive to cold. It was thought that he was hypothyroid but his basal metabolic rate was normal (0). However, his oral glucose tolerance test yielded a conspicuously flat curve. The fasting value was 75 mg., half-hour value 92 mg., two-hour value 73 mg., and three-hour value 68 mg. per 100 cc. His intravenous glucose tolerance test also yielded values below the normal range as established by Lozner, Winkler, Taylor, and Peters.[9]

Subsequently oral glucose tolerance tests were carried out on 20 patients with therapy-resistant T. rubrum infection. The intravenous test was done on six patients. Of the 20 patients, 8 had unusually increased oral tolerance (low or flat curves) with a peak value of 105 mg. per 100 cc. or less. Five showed a less pronounced but still conspicuously increased tolerance with a peak value of 122 mg. per 100 cc. or less. Six were normal, and one had slightly elevated tolerance. In intravenous testing only one additional patient showed abnormally low values throughout as did our first patient. Still, the fact remained that with oral testing more than half the patients showed an unusual type of curve.

Unfortunately, in the literature of glucose tolerance tests, only the upper limits of normal values are well established because of their great significance in incipient diabetes. Nobody has ever dealt with abnormally "flat" curves; the lower limits of normal values in the glucose tolerance test are not established. Still, from a remark of Watson[10] it may be concluded that half-hour values as low as 115 mg. per 100 cc. are exceptional. We could not find any half-hour value lower than 112 mg. per 100 cc. in the literature of glucose tolerance tests in normal persons. Lennox[11] tested 31 normal persons and found one with a peak value of only 112 mg. per 100 cc. His next lowest peak value was 126 mg. per 100 cc. It is known that flat curves occur in hypopituitarism, in adrenal insufficiency, and in myxedema. Such endocrine disorders were not present in our patients. They did not have clinical signs of any of these diseases, and their basal metabolic rates were within normal limits. For all practical purposes these patients have been perfectly healthy persons. One can only assume that their increased glucose tolerance on oral testing is a constitutional peculiarity the nature of which is not understood.

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7. Muskatblit, E.: Observations on Epidermophyton Rubrum or Trichophyton Purpureum, Mycologica **25**:109, 1933.

8. Ayres, S., Jr.: Dermatophytosis Due to Trichophyton Purpureum with Monilia Infection of the Mouth, Arch. Dermat. & Syph. **51**:285, 1945.

9. Lozner, E. L.; Winkler, A. W.; Taylor, F. H. L., and Peters, J. P.: The Intravenous Glucose Tolerance Test, J. Clin. Invest. **20**:507, 1941.

10. Watson, B. A.: Normal Glucose Tolerance Tests, J. Lab. & Clin. Med. **23**:364, 1938.

11. Lennox, W. G.: Repeated Blood Sugar Curves in Non-Diabetic Subjects, J. Clin. Invest. **4**:331, 1927.

POSSIBLE SIGNIFICANCE OF INCREASED GLUCOSE TOLERANCE

The question arises as to whether this peculiarity can be linked in any way to the susceptibility towards T. rubrum and/or to the intractability of the infection.

Little is known about carbohydrate metabolism of the skin, but it is well established that hyperglycemia causes considerable increase in the glucose content of the skin in man and animals. Also, it is known that after administration of a single dose of glucose or other carbohydrates the skin glucose level remains elevated for three hours or longer.[12] When a person ingests carbohydrates with three or four meals per day, his cutaneous glucose level almost continuously will be considerably higher than the fasting value. Persons whose blood sugar does not rise or rises only a little after ingestion of carbohydrates possibly will have a lower average glucose content in their skin (and in their horny layer) than persons with a normal degree of alimentary hyperglycemia.

Dermatophytes metabolize glucose preferentially, but they can adapt themselves to glucose-free media. Then they are able to burn nitrogenous material and do so in the absence of glucose.[13] There is some evidence [14] that fungistatic agents inhibit growth of fungi by interfering with their carbohydrate utilization. Therefore, it is feasible that, also in vivo, fungi thriving in a medium with low glucose content adapt themselves to utilize nitrogenous material. In this case they will be able to withstand the effect of fungistatic agents more than when glucose is present in abundance. This might be the case in our patients with low-grade alimentary hyperglycemia.

This hypothesis is now being tested by in vitro experiments, but the results so far have been inconclusive.

THERAPEUTIC EXPERIMENTS

Thyroid Medication.—Our working hypothesis implied that the responsiveness of the fungous infection to treatment would improve if the alimentary hyperglycemia could be raised in our patients. We attempted to do that by administration of thyroid on suggestion of Dr. Henry T. Ricketts of the Section for Metabolic Diseases, School of Medicine, University of Chicago. The therapeutic results were inconclusive. However, in several cases the impression was that the disease of palms and soles could be better controlled clinically when thyroid was administered together with local application of fungistatic agents. The nail infection remained unchanged. The following case illustrates the point.

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12. Folin, O.; Trimble, H. C., and Newman, L. H.: The Distribution and Recovery of Glucose Injected into Animals, J. Biol. Chem. **75**:263, 1927. Urbach, E., and Sicher, G.: Beiträge zu einer physiologischen und pathologischen Chemie der Haut: Der Zuckergehalt der Haut unter physiologischen und pathologischen Bedingungen, Arch. Dermat. u. Syph. **157**:160, 1929. Matsumoto, Y.: An Experimental Study of the Carbohydrates of the Skin with Special Reference to the Combined Sugar (Protein Sugar) and the Glycogen, Mitt. a. d. med. Akad. zu Kioto **8**:481, 1933. Sellei, C., and Spiera, M.: Die Rolle der Haut im Kohlehydratstoffwechsel, Biochem. Ztschr. **296**:83, 1938. Cornbleet, T.: Cutaneous Carbohydrates: I. The Normal Skin, Arch. Dermat. & Syph. **41**:193, 1940. Urbach, E., and Lentz, J. W.: Carbohydrate Metabolism and the Skin, ibid. **52**:301, 1945.

13. Melton, F. M.: The Effect of Various Substances on the Oxygen Uptake of Microsporum Canis Growing in Submerged Culture, J. Invest. Dermat. **17**:27, 1951.

14. Grunberg, E.; Soo-Hoo, G.; Titsworth, E.; Ressetar, D., and Schnitzer, R. J.: Mycological Studies with a New Benzothiazole with Specific Activity Against Dermatophytes, Tr. New York Acad. Sc. **13**:22, 1950.

CASE 2.—A 38-year-old housewife was first seen in the University of Chicago Clinics on Oct. 14, 1948. She had had hyperkeratotic T. rubrum infection of palms, soles, fingernails, and toenails which started on the feet 20 years ago. She had been treated with a great number of fungistatic agents, with x-rays, and by surgical evulsion of the nails. In our clinic she was treated with local applications of sulfur-salicylic ointments (concentrations up to 30% salicylic acid and 20% sulfur), ammoniacal silver nitrate paints, 5% chrysarobin ointment, and 5% asterol® (2-dimethylamino-6-[β-diethylaminoethoxy]-benzothiazole dihydrochloride) ointment for over two years. The beneficial effect of all these applications was negligible, and the lesions continued to contain fungi. The patient was placed on thyroid therapy on Dec. 29, 1950. She was given 1-grain thyroid tablets three times a day. Asterol® ointment was applied the same way as before. Inasmuch as her basal metabolic rate remained unchanged, this therapy was continued for nine months. As early as two weeks after initiation of this therapy, the scaling of the palms subsided completely, and the soles improved greatly. The palms have remained clear ever since; the soles cleared up completely four months later. Palms and soles have become and remained mycologically negative. However, the nails have not responded, and all nail fragments still yield positive fungus findings despite continuous treatment.

Local Treatment.—When it became obvious that the results of thyroid medication were equivocal and that the nail infection was not influenced by it, we attempted to use concentrated lithium bromide solutions locally, after it was found that the permeability of hard keratin structures can be greatly increased by such treatment.[15] Patients were advised to soak their nails by applying to the nail plates cotton pads moistened with the following, preferably warm, solution:

Formula 1	
Lithium bromide	75.0 gm.
Water to make	100.0 cc.

Soaking was done for one-half to one hour every night. After the soaks, a nail lacquer of the following composition was applied to the nails:

Formula 2	Gm. or Cc.
Clear nail lacquer	630.4
Lithium bromide	108.0
Alcohol 85%	120.0
Water	48.0
Asterol® base	57.6

This lacquer [16] was left on the nails for 24 hours and removed with nail polish remover just before the soaking was done again the following evening.

Some patients tolerated warm lithium bromide soaks well also on palms and soles. Some were able to immerse their hands and feet in the warm solution without irritation for shorter or longer periods. But in some patients we had to be careful to have the cotton pads applied exactly to the nail plates only, otherwise inflammatory irritation occurred in the paronychial tissue and/or elsewhere on the skin.

Lately, on the basis of our working hypothesis we tested the effect of varying concentrations of glucose on T. rubrum in vitro and found that very high glucose concentrations such as 20 or 30% are harmful, particularly to strains which were previously kept on a glucose-free medium. Therefore, an attempt was made to interfere with the metabolism of the fungi in skin and nails by spraying a highly concentrated glucose solution with an added water-soluble fungistatic agent to skin and nails prior to the application of the nail lacquer. The solution was prepared as follows:

15. Rothman, S., and Taschdjian, C. L.: A New Method to Increase the Permeability of Hard Keratin Structures, J. Invest. Dermat. **17**:9, 1951.

16. Supplied by Hoffmann-La Roche, Inc.

Formula 3: Place 100 gm. of glucose in a pyrex® flask calibrated at 100 cc. and add water while shaking to the 100-cc. mark. Boil the syrup until all glucose is dissolved. Add 10 cc. of the warm solution to 50 cc. of 5% asterol® tincture. The final concentrations in this solution are roughly 13% glucose and 4% asterol.®

At present we are using a combined method of treatment of the nails. First we apply the lithium bromide soaks (Formula 1); subsequently we spray the glucose-asterol® solution on the nails (Formula 3), and finally when the solution has dried, the lacquer (Formula 2) is painted on the nail plates. After 24 hours the lacquer is removed with nail polish remover, and the whole procedure is repeated.

Fig. 1.—Dermatomycosis pedis and nail infection of 25 years' duration in 48-year-old man. *A*, before treatment; potassium hydroxide positive; T. rubrum cultured. *B*, after treatment; skin and nails free of fungi for nine months microscopically and culturally.

For treatment of palms, soles, and other sites with hyperkeratotic lesions we try lithium bromide soaks as tolerated. Soaks are followed by spraying of the glucose-asterol® solution. After this solution has dried 5% asterol® ointment is massaged into the skin. The application of some greasy material is required because of the considerable drying effect of the lithium bromide and glucose solutions.

The results with this method have been encouraging, although it appears that the treatment has to be continued for many months. Initially the lithium bromide

in the soaks and in the nail lacquer causes an almost complete dissolution of the nail plates, particularly on toenails, and it takes a long time until the new healthier-looking plate becomes visible at the proximal end of the nail bed. Because of the long duration and exacting nature of the treatment and because of the initially slow results, we have lost several patients throughout the experimental period. At present nine patients return regularly for observation, mycologic examination, and treatment. All of them are clinically improving and have decreasing numbers of positive mycologic findings. We believe that by addition of glucose sprays the rate

Fig. 2.—Mycosis of right palm and fingernails of four years' duration in 61-year-old woman. *A*, before treatment; potassium hydroxide positive; T. rubrum cultured. *B*, after treatment; palm and nails free of fungi for three months.

of improvement has been accelerated. Three out of these nine patients can be tentatively regarded as cured of their dermatophytosis and onychomycosis. After two, eight, and four months, respectively, these three patients showed clinically normal skin and normal nail plates (Figs. 1, 2, and 3). At this writing they have been microscopically and culturally negative for nine, three, and three months, respectively.

Under the influence of continuous lithium bromide application, the newly growing nail is more convex, has a larger lunula, and is thicker than a normal nail.

It may become quite thick and hard on the fingers, whereas it remains relatively soft on the toes apparently because of water-proof covering by the shoes. The thickening of the nail persists as long as the lithium bromide is being applied; it also persists on nails which do not harbor fungi any more. As long as lithium bromide soaks are used, the paronychial tissue is usually macerated (Fig. 3).

We have not yet tried to discontinue entirely treatment of the patients who have become mycologically negative. Whether relapses will occur remains to be seen.

It should be emphasized that so far we have not carried out controlled experiments testing the relative efficacy of the materials used. Especially, we do not know whether the same results could not be obtained without addition of fungistatic agents. In vitro experiments indicate [15] that concentrated lithium bromide solutions in themselves are fungistatic. The same is true for highly concentrated glucose solutions.

Fig. 3.—Onychomycosis of fingernails of 10 years' duration in 39-year-old man. *A*, before treatment; potassium hydroxide positive; T. rubrum cultured. *B*, after treatment; nails free of fungi for three months. Maceration of paronychial tissues is due to lithium bromide treatment. No fungi were demonstrable in these areas.

SUMMARY

In 13 out of 20 cases of recalcitrant Trichophyton rubrum (purpureum) infections of palms, soles, and nails, an increased glucose tolerance was found on oral testing.

A working hypothesis is presented postulating that if the glucose content of the skin and the horny layer is low, the fungi adapt themselves to metabolize substances other than glucose and thereby become more resistant to fungistatic agents which primarily inhibit carbohydrate utilization.

Thyroid medication when combined with application of fungistatic agents seems to promote the cure of the infection on the skin but not on the nails.

Combined local application of a fungistatic agent, concentrated lithium bromide, and concentrated glucose solutions resulted in disappearance of the onychomycosis in three out of nine patients after treatment was continued for several months. The other six started to grow healthy nail plates but are still mycologically positive.

Dr. Eugene J. VanScott, National Cancer Institute, Public Health Service, Federal Security Agency, assisted in this study.

GENERALIZED TRICHOPHYTON RUBRUM INFECTION ASSOCIATED WITH SYSTEMIC LYMPHOBLASTOMA

Report of Three Cases

GEORGE M. LEWIS, M.D.

MARY E. HOPPER, M.S.

NEW YORK

AND

MICHAEL J. SCOTT, M.D.

SEATTLE

OUR INTEREST in this subject dates from 1945, when a patient who later died of leukemia presented a generalized erythroderma considered at first to be specifically and solely related to the blood dyscrasia. However, scrapings from multiple sites revealed filaments, and on culture Trichophyton rubrum (purpureum) was isolated. Since then two additional cases of lymphoblastoma have been observed in which widespread T. rubrum infections were coincidentally present.

OTHER FUNGI AND LYMPHOBLASTOMA

The observation of Fitchett and Weidman,[1] reported in 1934, that tissue from a patient with Hodgkin's disease yielded a colony of fungus diagnosed as Cryptococcus (Torula) histolytica, raised the question of a possible close association of apparently dissimilar diseases. Some of the culture was injected into the meninges of a cat, and a picture like that of Hodgkin's disease was reproduced histologically. This suggested that Hodgkin's disease might have a fungal origin. However, that possibility has not been confirmed. Independently and at about the same time, Mallory [2] mentioned that he had observed four cases in which Cryptococcus infection and Hodgkin's disease were present in the same patient and one instance of cryptococcosis and lymphosarcoma. He stated that there were 12 additional cases in the literature of coexistant cryptococcosis and Hodgkin's disease. The report of Cawley and Curtis [3] in 1948, in which they reviewed the statistics of Miller, Keddie,

From the Department of Medicine (Dermatology), New York Hospital and Cornell University Medical College.

Read at the Seventy-Second Annual Meeting of the American Dermatological Association, Inc., Colorado Springs, Colo., April 24, 1952.

1. Fitchett, M. S., and Weidman, F. D.: Generalized Torulosis Associated with Hodgkin's Disease, Arch. Dermat. & Syph. **18**:225 (Aug.) 1934.

2. Mallory, T. B., in Case Records of the Massachusetts General Hospital, Case 20241, New England J. Med. **210**:1293 (June 14) 1934.

3. Cawley, E. P., and Curtis, A. C.: Histoplasmosis and Lymphoblastoma: Are These Diseases Related? J. Invest. Dermat. **11**:443 (Dec.) 1948.

Johnstone, and Bostick,[4] and four case reports by Riehl,[5] Williams and Cromartie,[6] Parsons and Zarafonetis,[7] and Miller and associates [4] brought up a second possible relationship betwen a fungus and a lymphoma. The association which they noted was between leukemia and histoplasmosis (in two cases) and Hodgkin's disease and histoplasmosis (in two cases). As Cawley and Curtis pointed out, four instances of coincidental occurrence of two rare disorders in a series of 88 cases of histoplasmosis is greater than can be accounted for by mere chance. They therefore believed that there might be a relationship between these disorders. They also pointed out that the reticuloendothelial system is involved by both histoplasmosis and the lymphoblastomas. It was their opinion that lymphoblastoma might predispose to histoplasmosis. They did not believe that an actual transition between the two diseases was likely. It was Weidman's belief [8] that preexisting granulomatous diseases might predispose to mycotic infection. Goldman [9] cited a case in which histoplasmosis and mycosis fungoides coexisted. Weidman [10] and Lever [11] both pointed out the difficulty sometimes encountered in distinguishing lymphoblastoma histologically from inflammatory reticuloendothelioses such as the invasive mycoses, tuberculosis, and syphilis.

A review of the literature fails to reveal any instance in which attention is drawn to a significant association between a superficial mycosis and lymphoblastoma.

REPORT OF CASES

CASE 1.—N. K., a 62-year-old white man, a native of Czechoslovakia, was observed first in the Dermatology Clinic of New York Hospital in July, 1945. He had been a diabetic for over 20 years. An eruption scattered over the trunk and extremities had appeared subsequent to a severe sunburn, 17 days before. On the patient's scalp, neck, trunk, and extremities, scaly, slightly lichenified, discrete and confluent lesions were present, with some satellite lesions beyond the periphery. The eruption was mildly inflammatory and suggested a fungous infection. Skin scrapings from several areas were positive for fungi in potassium hydroxide preparations. T. rubrum was isolated on culture. The patient failed to return for further therapy after his initial visit.

In November, 1947, he was admitted to New York Hospital because of progressive blurring of vision during the previous six months. The ophthalmologic diagnosis was chronic, noncongestive glaucoma. Upon hospital admission he had a generalized erythroderma with fine whitish scales. The skin was slightly lichenified, and a few excoriations were noticeable, although he stated the condition was asymptomatic. The generalized skin disorder was of six months' duration. The cervical, submental, epitrochlear, inguinal and femoral lymph nodes were firm,

4. Miller, H. E.; Keddie, F. M.; Johnstone, H. G., and Bostick, W. L.: Histoplasmosis: Cutaneous and Mucomembranous Lesions; Mycologic and Pathologic Observations, Arch. Dermat. & Syph. **56**:715 (Dec.) 1947.

5. Riehl, G., Jr.: Durch pathogene Sprosspilze bedingte Granulome, Arch. Dermat. u. Syph. **148**:392, 1925.

6. Williams, R. H., and Cromartie, W. P.: Histoplasmosis: Report of a Case, Ann. Int. Med. **13**:2166 (May) 1940.

7. Parsons, R. J., and Zarafonetis, C. J. D.: Histoplasmosis in Man: Report of 7 Cases and a Review of 71 Cases, Arch. Int. Med. **5**:1 (Jan.) 1945.

8. Weidman, F. D., in discussion on Curtis, A. C., and Grekin, J. N.: Histoplasmosis, J. A. M. A. **134**:1224 (Aug. 9) 1947.

9. Goldman, L., in discussion on Cawley and Curtis.[3]

10. Weidman, F. D., in discussion on Cawley and Curtis.[3]

11. Lever, W. F., in discussion on Cawley and Curtis.[3]

Fig. 1 (Case 1).—Generalized infection due to T. rubrum. *A*, in 1945 the eruption was widespread but superficial and noninfiltrated. *B*, in February, 1948, the patient was found to have leukemia cutis, but T. rubrum could also be demonstrated from widely selected samples. *E* and *D*, in May, 1948, two weeks before death, the mixed skin disorder was universal; edema of the extremities was extreme.

discrete and nontender. The axillary and inguinal lymph nodes were approximately 2 by 3 cm. in diameter. The liver was palpable three fingerbreadths beneath the right costal margin. Hematologic studies indicated lymphatic leukemia. Histologic examination of an axillary lymph node and a section of skin surgically removed from the chest confirmed this diagnosis. The topography of the lymph node was completely obliterated by large numbers of cells of the general appearance and size of lymphoblasts. These cells had very little cytoplasm but very prominent nuclei and were scattered in a haphazard fashion throughout the section. Small remnants of lymph follicles could occasionally be detected. Mitotic figures were not noted. The capsule of the node was almost entirely free from infiltration. A specimen stained by the

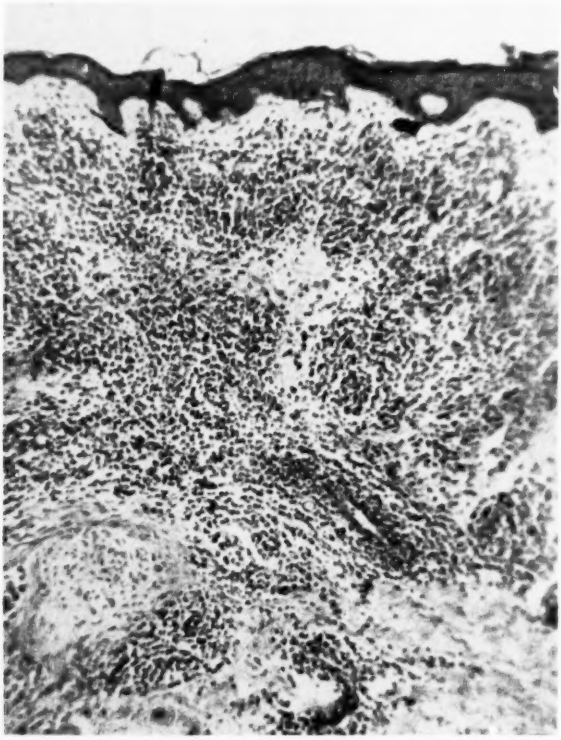

Fig. 2 (Case 1).—Section of skin showing extensive infiltrate throughout the entire upper half of the cutis. Higher magnification revealed the cells to be predominantly lymphocytic.

Giemsa method showed a node invaded by fat, with its topography largely obliterated by large numbers of lymphocytes. Scattered through these were occasional lymphoblasts, some of them in mitosis. A section fixed in Bouin solution and stained by the routine Masson method showed essentially the same features. The lymph channels were choked with lymphocytes, and numerous lymphocytes were seen in the blood vessels. A biopsy specimen of skin exhibited widespread deposits of the same type of cells in the corium. Silver impregnation of this section of skin showed that the lymphoid infiltration of the corium possessed a very abundant reticulum typical of the lymphoid variety. The general appearance of the lymph node and the skin was more compatible with leukemia than with lymphosarcoma.

At first the skin lesions were thought to be solely an expression of leukemia. However, when searched for, fungi could be demonstrated with ease from multiple skin samples. Cultures yielded T. rubrum in specimens from the face, ear, back, and abdomen. The trichophytin test gave negative reactions in 15 minutes and again after 48 hours.

An electrocardiogram and x-rays of the chest and abdomen were essentially negative. Serologic tests for syphilis were negative. Urinalyses often showed the presence of sugar. The thymol turbidity test was 3 units; sulfobromophthalein sodium excretion 3.1%; alkaline phosphatase 5.9 units; and serum protein 6.7 gm. with 3.9 gm. of albumin and 2.8 gm. of globulin per 100 cc. The clot retraction and clot fragility in 24 hours were reported as good. The bleeding time was two minutes; clotting time eight and a half minutes; the Rumpel-Leede test was negative. The prothrombin time undiluted was 12.8 seconds, diluted 35.1 seconds, and the standard control was 38.2 seconds.

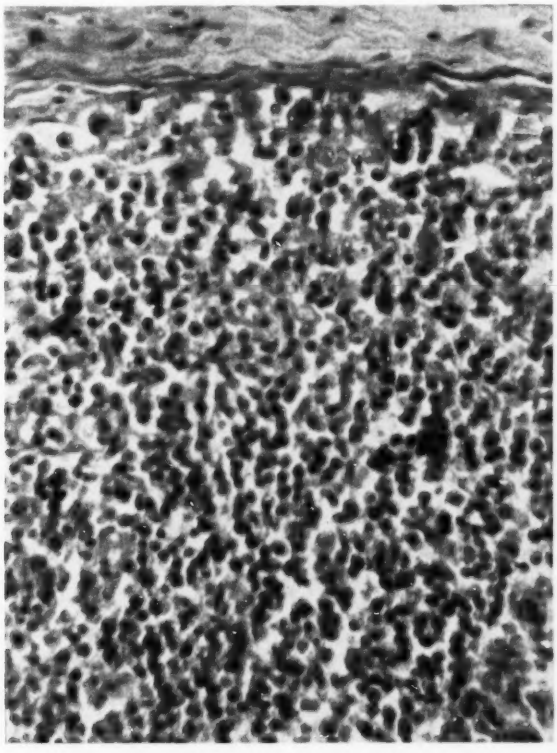

Fig. 3 (Case 1).—Section of lymph node showing capsule and solid mass of small dark cells, mostly mature in type, compatible with the picture of lymphatic leukemia.

Topical therapy consisted of various antipruritic and mildly fungicidal ointments. X-ray therapy had no demonstrable beneficial effects either on the cutaneous lesions or the lymphadenopathy. "Aminopterin" (4-aminopteroyl glutamic acid) was administered intramuscularly in daily doses varying from 0.5 to 4 mg. The diabetes was controlled by daily injections of 10 units of protamine zinc insulin and 20 units of regular insulin. The patient was discharged from the hospital in December, 1947. His course proved to be progressively downhill, and he was rehospitalized in April, 1948. At the time of this hospitalization his entire skin was erythematous and covered with fine whitish scales. A + 2 pitting edema was the most striking clinical feature. Generalized lymphadenopathy was still present and the liver was still palpable. The physical examination was otherwise noncontributory.

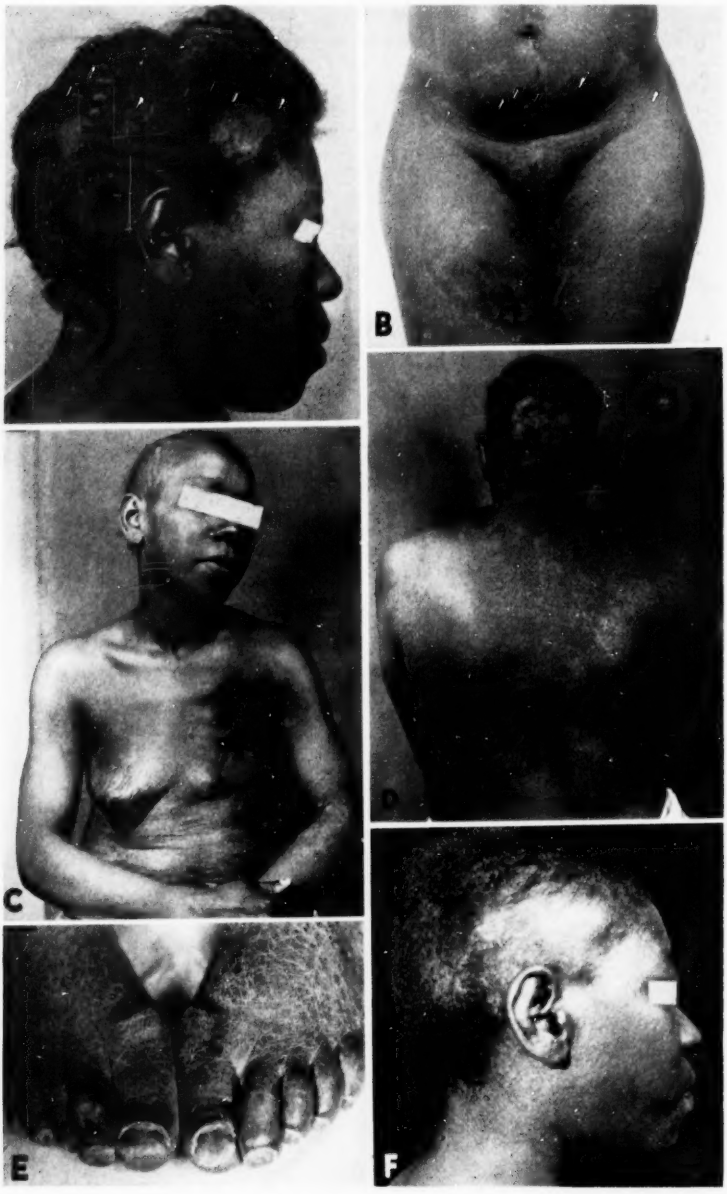

Fig. 4 (Case 2).—Skin infection due to T. rubrum. In 1949 the eruption was widely distributed as localized plaques: *A*, two areas of partial alopecia on scalp; *B*, showing tendency to affect chiefly the lower torso and thighs. In 1951 the infection had spread to involve approximately 75% of the total body area: *C*, showing mastectomy scar; *D*, diffuse eruption over the back. *E* and *F*, in 1952 the nails and feet were heavily affected; and the entire scalp and face were involved in a scaly erythroderma.

Hematologic findings were again characteristic of lymphatic leukemia, with many atypical cells. The electrocardiogram was recorded as being essentially normal. X-ray studies of the chest disclosed widening of the superior mediastinum. The urine occasionally contained sugar.

Tests revealed sulfobromophthalein sodium 24.6%; cephalin flocculation 6 units; phenolsulfonphthalein reaction 85% excretion; and the serum protein 5.8 gm. with 3.6 gm. albumin and 2.2 gm. globulin per 100 cc. A stool specimen reacted negatively to the guaiac test.

The patient failed to respond to therapy with stibophen (fuadin*), α-estradiol (progynon*), and mercurial diuretics. He gradually lapsed into coma and died on June 3, 1948, the 53d day after hospital admission.

An autopsy was performed. All the subcutaneous tissues were extremely edematous. Moderate pulmonary hyperemia, emphysema, and lower lobe atelectasis were present. Approximately 1,000 cc. of transudate with a specific gravity of 1.010 was removed from each pleural cavity. Histologic sections from an axillary lymph node showed the entire organ to be packed with a homogeneous mass of blast forms. Histologic sections of skin removed from the abdomen and legs revealed acanthosis with superimposed hyperkeratosis. A 2-mm. layer of loose vascular fibrous tissue densely infiltrated with blast cells was situated in the corium adjacent to the epidermis. The underlying corium was thickened and composed of dense collagen tissue. A blast cell infiltration was located around the sweat glands and hair follicles. The findings at autopsy confirmed the diagnosis of acute lymphatic leukemia.

It was thought that the superficial fungous disease preceded the development of leukemia, as there was no clinical evidence of the latter disease when the patient was first observed in 1945. The blood was not examined at that time but had been normal in 1940. Worth remarking on is the possible predisposing factor of diabetes known to have existed for 20 years prior to his first visit. The rapid onset of the mycosis is of interest, with the possibility of its precipitation by exposure to the sun.

Case 2.—J. M., a Negro woman aged 35, sought help in the Dermatology Clinic of New York Hospital in August, 1949. She complained of a gradually progressive, pruritic skin rash during the preceding two years. Her past history revealed an attack of rheumatic fever in 1938, hay fever since 1939, and asthma since 1948. In 1945 and 1949 Caesarean sections were performed. A left radical mastectomy for carcinoma was done in 1941.

In 1947 the patient noted a pruritic eruption in the inguinal region, bilaterally, with slow spread to the abdomen and thighs. An eruption also developed on the dorsa of the great toes and eventually involved the feet and ankles. For two months pruritus and tenderness were noted in two areas of the scalp. The hair subsequently gradually fell out in these patches.

A confluent, scaly lichenified, sharply demarcated eruption with serpiginous borders involved the back, axillae, left elbow, right breast, abdomen, inguinal regions, pubis, anterior and medial aspects of the thighs, and the gluteal fold. Similar discrete ovoid and circinate plaques up to 7 cm. in diameter were present on the abdomen. The dorsa of both great toes and adjacent portions of the feet were similarly involved. The distal portions of several toenails were opaque, yellowish, fragile, and separated from the nail bed. The fingernails were normal. In the posterior parietal and temporal portions of the right side of the scalp were two areas of partial alopecia approximately 4 cm. in diameter. No hair stumps were visible in the affected regions. The scalp hair did not fluoresce when examined in filtered ultraviolet rays. Potassium hydroxide preparations of skin scrapings from the scalp, thighs, and feet were positive for fungi. Cultures of T. rubrum was obtained from multiple areas, including the toenails.

The patient abruptly disappeared from observation and was not seen again until June, 1951. The skin eruption had continued to spread, with new lesions in previously uninvolved sites, despite the application of various proprietary ointments. The entire scalp and pubis were almost devoid of hair. Numerous minute follicular papules were noted throughout the scalp. Well-demarcated, scaly, moderately lichenified patches of dermatitis with irregular serpiginous borders were present on the neck, arms, trunk, thighs, legs, and feet. The individual lesions were up to 25 cm. in diameter. The toenails exhibited the characteristic signs of onychomycosis, as on her initial visit, but the fingernails were not affected.

Potassium hydroxide preparations of skin scrapings from the scalp, back, arm, and knee were all positive for fungi. Cultures of T. rubrum were obtained from all these areas. The int..acuta-

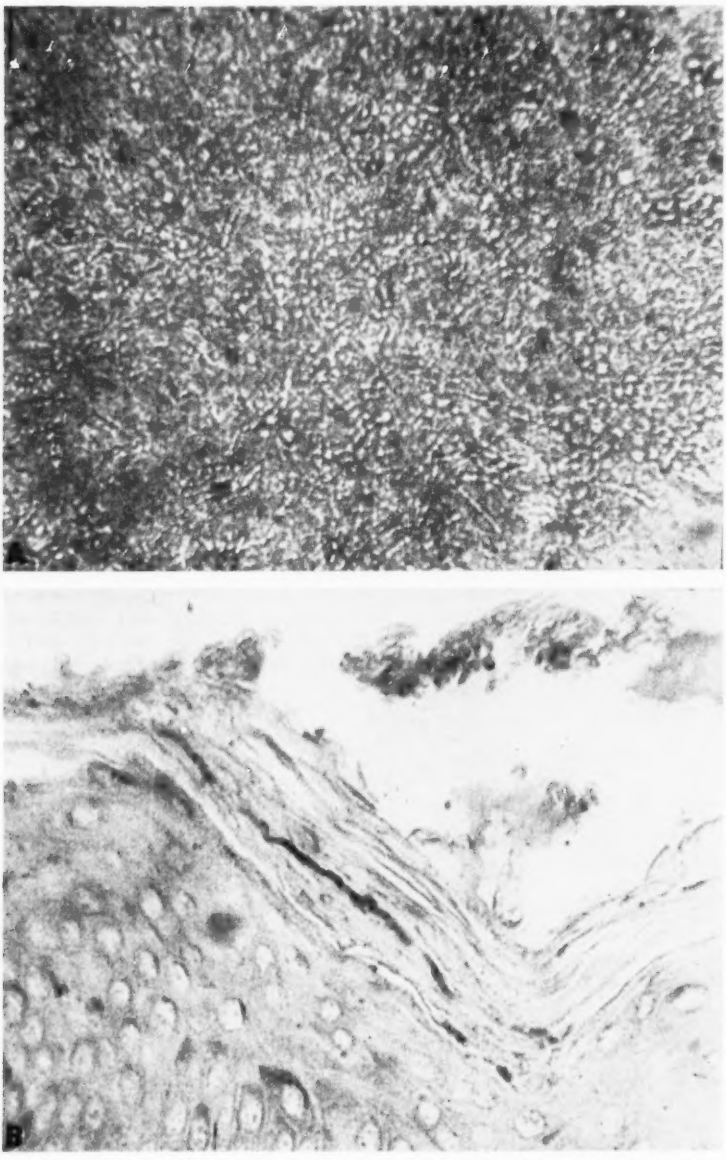

Fig. 5 (Case 2).—*A*, solid mass of fungous filaments and spores in a specimen made from a thick scale. *B*, section of skin showing fungous filaments deep in the stratum corneum; Hotchkiss-MacManus stain.

neous test with trichophytin produced a wheal reaction within five minutes and no reaction after 48 hours. Histologic examination of cutaneous tissue surgically removed from the scalp and the arm demonstrated mycelia in the stratum corneum. The Hotchkiss-McManus stain was utilized for the preparation of these specimens.

Because of dyspnea in April, 1950, a thoracic operation was performed at Memorial Hospital. A large mediastinal mass with pulmonary and pleural nodules was discovered at operation. Biopsy specimens taken from the diaphragm and pulmonary nodules were reported as showing: (1) small cell lymphoblastoma; (2) lymphosarcoma, and (3) a few clumps and strands of carcinoma (considered to be metastatic).

It was a recent opinion of Dr. Fred Stewart, Memorial Hospital, that the primary disorder was some form of epithelial tumor with a great deal of lymphoid reaction. Dr. Charles Olcott, Cornell University Medical College, concurred in this opinion.

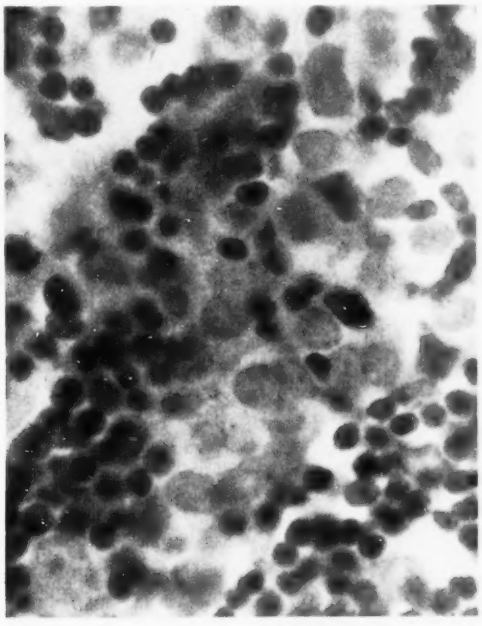

Fig. 6 (Case 2).—Section from nodule in mediastinum. In the lower left-hand corner a large irregular anaplastic (carcinoma) cell is seen. The bulk of the cells are mature lymphocytes with some large histiocytes.

At Bellevue Hospital in August, 1950, a course of nitrogen mustard therapy had to be discontinued because of leukopenia.

A roentgenogram of the chest showed a large oval air-containing pocket in the midportion of the right lung field measuring approximately 7 by 4.5 cm. It extended from the lung root to the lateral chest wall. The pulmonary parenchyma above this level contained little air. The portion of the lung below this level was better aerated, but the pulmonary markings were close together. Because of the distortion of anatomy, the possibility of enlarged mediastinal nodes could not be determined. Hematologic examinations revealed the hemoglobin to be 11.8 gm., and the red blood cell count was 5,100,000. The white blood cell count was 10,300, with a differential count of 67% polymorphonuclear neutrophiles, 27% lymphocytes, 4% monocytes, and 2% eosinophiles. The remaining laboratory data were essentially negative.

Subsequent Course.—There has been progressive physical deterioration, and in April, 1952, she was able to work only part time. Filtered roentgen therapy (5,400 r) was administered to the right chest in 1950. The lymphoblastoma (lymphosarcoma) has shown no apparent progression. The skin disease has been relentlessly present. The eruption is similar to that already noted as a well-demarcated plaque-like rash of generalized extent. The borders are frequently thickened and elevated. In addition, localized, painful nodosities have been present at various times in the substance of involved tissue on the extremities. A biopsy of such a lesion in the right leg revealed a follicular, necrotic response to T. rubrum. The organism was present in the tissues around the hair shaft.

Case 3.—A. S., a white man, aged 71, a patient of Dr. Maurice J. Costello, was first observed on May 7, 1951. He was a lawyer of German-French ancestry. A gradually spreading eruption had first appeared 16 months previously, for which he had been treated by ointments and by the oral administration of tablets. The eruption was generalized, completely covering the neck, shoulders, arms, and torso. The lower part of the back, the forearms and the hands, the buttocks, thighs, legs, ankles, and soles were affected by nummular and geographic patches; large plaques were present on the buttocks and thighs. The bearded region was studded with pea-sized inflammatory, edematous, nodose lesions. The generalized eruption was erythematous, edematous, and scaly, with a sharp and, at times, elevated border characteristically serpiginous in outline. The fingernails were dull, friable, and dystrophic. There was no fluorescence of the scalp hair or beard under filtered ultraviolet light. The tongue was bald, and the usual orange fluorescence was absent. Skin scrapings revealed fungi, and on culture T. rubrum was isolated. The trichophytin test was positive, with a whealing reaction in 15 minutes, but negative after 48 hours.

Two urinalyses were normal. The blood sugar level was 92 mg. per 100 cc. An examination of the peripheral blood in June, 1951, gave the following results: hemoglobin 86% (12.9 gm.); red blood cells 4,100,000; white blood cells 8,500; polymorphonuclears 68%; lymphocytes 25%; monocytes 6%; eosinophiles 1%. Platelets were plentiful.

Local therapy with benzoic and salicylic acid (Whitfield's) ointment, anthralin ointment, and asterol® dihydrochloride ointment and solution appeared to effect moderate improvement after four months. In September, 1951, the patient stated that for three weeks he had suffered from pain in the left chest, the left shoulder, and the left arm. Shortness of breath developed on slight exertion; he was becoming increasingly weak, was pale, and had a rapid pulse. He was referred to his personal physician, Dr. Robert Shearman, who had the patient admitted to the Methodist Hospital, Brooklyn.

A tumor mass was found in the left anterior mediastinum. Palpable lymph nodes were present in the cervical and axillary regions. On Sept. 24, the day of admission, a blood count revealed the red blood cells to be 1,400,000; the white blood cells 10,000; polymorphonuclears 69%; lymphocytes 29%, and basophiles 2%. Subsequent counts confirmed this severe anemia, which failed to respond after repeated transfusions of whole blood. The white blood cell count on Oct. 22 was 7,800. Subsequent counts revealed leucopenia with a count varying between 4,200 and 2,500. There was a progressive increase in the number of monocytes; on Jan. 3, the percentage of monocytes was 37. The blood sedimentation rate was 150 mm. per hour. The fasting blood sugar was 91 mg.; nonprotein nitrogen was 35 mg. per 100 cc.; guaiac test of feces 1+; the Wassermann reaction was negative, and urinalysis was repeatedly normal.

A lymph node biopsy revealed a chronic lymphadenitis with some hyperplasia. The sternal marrow was studied by Dr. Nathan Rosenthal, who reported that "the bone marrow shows a marked hypocellularity. No megakaryocytes were found in the smear. The thicker portions of the smear showed the presence of large numbers of reticulum cells with myeloblasts and promyelocytes. These findings are very suggestive that the underlying condition is that of reticulum cell leukemia. Another striking finding in the marrow is the complete absence of nucleated cells (erythrocytopenia), which undoubtedly accounts for the severe anemia as a result of lack of red cell formation."

A course of high voltage, filtered x-ray therapy, consisting of 11 exposures during the period between Nov. 21, 1951, and Dec. 14, 1951, was administered to an area 15 by 15 cm. over the left anterior chest. No reduction in the size of the mediastinal tumor occurred.

An exploratory operation was decided upon, and a small section of the tumor was removed. Dr. Bayard S. Herr Jr., Amsterdam, N. Y., considered this to be a teratoma and to have no relation to the hematologic condition. The lesion was considered inoperable.

Continued symptomatic therapy, including transfusions, was undertaken, but the patient gradually became weaker and on Jan. 28, 1952, he died. Ten days before his death the white blood count was 10,900 and it gradually increased to 30,000 on the day he died. The differential count showed a predominant number of polymorphonuclear leucocytes.

Permission for autopsy was not obtained. The final impression was teratoma of the mediastinum and monocytic leukemia.

COMMENT

At first, we might dismiss the simultaneous presence of two apparently unrelated disorders as a chance association and of no significance. On reflection, this seems less and less likely, since lymphoblastoma is uncommon and generalization of T. rubrum infections is also decidedly infrequent, at least in New York.[12] Our records indicate only six other cases in which the fungous disorder was of widespread distribution during the past 12 years in which our laboratory has been in

Summary of the Three Case Reports

	Case 1	Case 2	Case 3
Age	62	35	71
Sex	M	F	M
Duration of mycosis prior to discovery of lymphoma	2 yr.	2 yr.	20 mo.
Possible predisposing factor	Diabetes? Sunburn?	Carcinoma?	None
Trichophytin test			
15 min.	Negative	Positive	Positive
48 hr.	Negative	Negative	Negative
Nature of lymphoma	Acute lymphatic leukemia	Lympho-sarcoma?	Monocytic leukemia
Additional neoplasm	None	Carcinoma	Teratoma
Result	Death	Health poor	Death

operation at New York Hospital. Even if we assume that these patients are in a satisfactory state of health, the fact still remains that the percentage of concomitant disease is too high to be considered coincidental.

The next, and at present the best, explanation for the dual presence of fungous and lymphogenous diseases is that the systemic disorder lowers the resistance of the host sufficiently to predispose to the more active invasion of the mycotic agent. This was considered an adequate reason for the invasion of Cryptococcus neoformans and Histoplasma capsulatum by Weidman and others, as already noted. If this was accepted for T. rubrum, it would remove it from the obligatory superficial infections and place it with Candida (Monilia) albicans in an intermediate group with the feature of more active invasion in the presence of diseased tissue.

The variability of T. rubrum in its clinical manifestations is becoming increasingly apparent since the usual syndrome was first described.[13] While decidedly

12. Harris, J. H., and Lewis, G. M.: Trichophyton Purpureum (Bang) as a Deep Invader of the Skin, Arch. Dermat. & Syph. **22**:1 (July) 1930.

13. Lewis, G. M.; Montgomery, R. M., and Hopper, M. E.: Cutaneous Manifestations of Trichophyton Purpureum (Bang), Arch. Dermat. & Syph. **37**:823 (May) 1938.

uncommon, a case of hair follicle infection (ectothrix) was reported first in 1930 by Harris and Lewis. This has been substantiated by a skin biopsy in Case 2 in this communication. Another case of interest is that of a patient with eosinophilic granuloma,[14] who had a moderately severe dermatophytosis of the feet and toenails due to T. rubrum. Cure of the granulomatous eosinophilic disease was finally achieved after the administration of large doses of potassium iodide over a period of several months. This did not apparently affect the fungous disease. A review of his biopsy sections with use of the Hotchkiss-McManus stain failed to reveal fungi in the granulomatous tissues. However, it should be pointed out that part of the histologic picture of the eosinophilic granulomas included obliteration of many smaller blood vessels. This brings us to another interesting speculative field in which Thompson [15] led the way. It was his belief that evidence indicated a close parallelism between the presence of thromboangiitis obliterans and T. rubrum infection of the feet. Meyer [16] supported this thesis. In spite of negative experimental proof by Reiss and Graham,[17] Thompson's work still merits attention and may well be an additional link in the chain of evidence that T. rubrum has potentialities for at least limited invasion of the body. Using the Hotchkiss-McManus stain, we have searched carefully for fungi in biopsy specimens of various lymphomas. In no case have we been able to see any evidence of filaments or reproductive forms. Another interesting speculation is whether generalized T. rubrum infections have been overlooked and misdiagnosed as instances of dermatitis exfoliativa, psoriasis, neurodermatitis, pityriasis rubra, premycosis fungoides, and even leukemia cutis (as occurred in our first case). It is our impression that this occurs very seldom as the fungous disease is almost always plaque-like in part of its manifestation and would not likely be overlooked by an alert dermatologist. The vagaries of the disease, however, must be kept in mind, with the possibility of a mixture of diseases, particularly when a lymphoblastoma is recognized. It may also be pointed out that T. rubrum infections may simulate such a disorder as dermatitis herpetiformis, although the scalloped outlines of the plaques and other evidence of the disease in more typical form, such as on the feet or nails, should be sufficient to point to the correct diagnosis.

SUMMARY AND CONCLUSIONS

Three cases of widespread cutaneous involvement with T. rubrum are reported. A coexistant lymphoblastoma was present in each case (lymphatic leukemia, lymphosarcoma, and monocytic leukemia, respectively).

The generalization of the cutaneous mycosis was considered to be related, in part at least, to the underlying lymphoma. The possibility of chance association

14. Lewis, G. M., and Cormia, F. E.: Eosinophilic Granuloma: Theoretic and Practical Considerations Based on the Study of a Case, Arch. Dermat. & Syph. **55**:176 (Feb.) 1947.

15. Thompson, K. W.: The Relationship of the Dermatomycoses to Certain Peripheral Vascular Infections, Internat. Clin. **2**:156 (June) 1941; Studies on Relationships of Dermatomycosis to Ulceration and Gangrene of Extremities, Yale J. Biol. & Med. **16**:665 (July) 1944.

16. Meyer, N.: The Causative Relationship of Dermatophytosis to Thrombo-Angiitis Obliterans, Am. J. Med. Sc. **202**:822 (Dec.) 1941.

17. Reiss, F., and Graham, J. B.: Absence of Thrombo-Angiitis Obliterans in Experimental Dermatophytosis, J. Invest. Dermat. **7**:127 (June) 1946.

was considered remote, and no evidence was produced that T. rubrum was capable of causing the lymphatic disease, although its capability for limited spread was discussed.

The similarity of T. rubrum infections to neurodermatitis, psoriasis, and mycosis fungoides may lead to an error unless widespread and atypical manifestations are studied mycologically. Pruritus is common with all these dry, red, scaly disorders.

As an incidental finding, T. rubrum was shown to be an ectothrix invader of scalp hair and also the cause of small, painful abscesses as the result of invasion of hair follicles in the otherwise usual plaque-like involvement.

Dr. Maurice J. Costello gave permission to report the details concerning the third patient.

ABSTRACT OF DISCUSSION

ON PAPERS BY DR. ROTHMAN AND BY DRS. LEWIS, HOPPER, AND SCOTT

DR. FRED WEIDMAN, Philadelphia: In one of Dr. Rothman's lantern slides showing psoriasis-like gyrations, the surface appeared honeycombed, like favus. Both Trichophyton (Anchorion) gypseum and Trichophyton violaceum can cause favus; this dermatosis is not an etiologic entity; it is a clinical one. As I recall, a suppurative folliculitis was present, and, of course, this would augment the idea of favus.

It is Dr. Rothman's thesis that fungi growing in the low hydrocarbohydrate environment of cutaneous soil adapt themselves by utilizing protein. I take it that he means that the mechanism is similar to that which operates in body tissue cells in diabetes and which results in the formation of ketones. Perhaps he would imply that the substances produced by the fungi are of that order but, of course, not precisely these ketone substances. Could these ketone-like substances be the factors responsible for the recalcitrance?

At one time I applied glucose soaks to patches of dermatophytosis with the idea of changing the morphology of the parasite, and was unsuccessful. I did succeed, though, in securing special proliferation of the fungous cells, and in some cases in which it had been difficult to demonstrate the fungus microscopically, I found that after applying the glucose soaks the fungus could be demonstrated. According to Dr. Rothman's thesis, perhaps we have a case for glucose soaks in that they would appease the hunger of T. rubrum to such an extent that it would no longer draw upon human tissues, and therefore, no longer follow its "recalcitrant" type of life.

I was intrigued by the use of lithium bromide. I should like to have Dr. Rothman enlighten us as to why he "hit upon" it particularly. Was it a matter of trial and error of many, many substances? In that connection, methyl salicylate (wintergreen oil) is also an excellent penetrating agent. All of us are familiar with some of the museum specimens (Spalteholz preparations) in our medical schools in which embryos are cleared by it and the vascular trees, etc., revealed. Methyl salicylate, I think, has been neglected as a possible penetrating agent. Over and above this, it is fungicidal very much as are cinnammon oil and thyme oil. Kingery, Templeton, and Thienes have claimed the value of essential oils.

Finally, and most important, has Dr. Rothman thought of the possibility that T. gypseum infections might likewise show the flat glucose tolerance test; that is, that they should be run as a control series? If so, Dr. Rothman's thesis falls.

As to Dr. Lewis' paper, I think that the case is quite clear as to some kind of interrelationship between the two disease groups, that is, fungous disease on the one hand, and the lymphoblastoma-Hodgkin's disease group on the other. He brought out adequately the comparative rarity of both groups and, therefore, their significance statistically. It is a more difficult proposition as between the lymphoblastomas and the ubiquitous superficial dermatophytic conditions. He covers this point to some extent by quoting the rarity of T. rubrum infection in the New York area. This is a surprise to me, but I must accept it. Dr. Van Studdiford tells me of the numerous cases in New Orleans, and, accordingly, I should say that the New Orleans dermatologists are in the best position to pass on that point.

In the final analysis, in order to effect a lymphoblastomatous state we must assume that the fungi provoke a reticuloendothelial hyperplasia. I think that all of us are satisfied that super-

ficial involvement is not likely to do this. Allergic mechanisms in general are the more pronounced where the allergen is introduced more deeply. For the sake of Dr. Lewis' thesis, I was gratified when Dr. Lewis showed the illustration of the Hotchkiss-McManus reaction deep down in the hair follicle. That is the kind of case which I could more readily accept in support of the thesis which Dr. Lewis has offered.

In respect to the work of Thompson on Buerger's disease and dermatophytosis, Dr. Naide at the University of Pennsylvania supported much of his work. But, as I recall, Thompson himself has recanted from his original thesis that dermatophytosis is a cause of Buerger's disease.

DR. ARTURO L. CARRIÓN, San Juan, Puerto Rico: Infections with T. rubrum are of interest to me because of their high incidence in Puerto Rico, where they are registered in a proportion of approximately 5% of all dermatological cases. In an illustrated report published in 1930, I presented different clinical types of this mycosis as observed in our tropical country, including tinea cruris, tinea pedis, generalized eruptions, onychomycosis, and even tinea capitis. From more recent experience, tinea barbae may now be added to that list.

Dr. Lewis has raised the question of possible relationship between T. rubrum infections and the lymphoblastomas, as suggested by coincidental clinical observations. The implications of such a relationship, if confirmed, would be so far-reaching that further research toward the elucidation of that possibility should be encouraged. Clinically, T. rubrum has been found to produce intensive antigenic reactions on the human skin. The reaction of other tissues to the absorbed products of this fungus is still an open field for investigation.

In reference to Dr. Rothman's paper, it is interesting to know of his observations which tend to link treatment resistance in T. rubrum infections with altered metabolic conditions on the part of the host.

Allow me to give you my personal experiences regarding the treatment of this mycosis. I still believe that benzoic and salicylic acid ointment is the best therapeutic preparation against infections with this parasite. There is no doubt about the existence of a group of cases that do not respond to any known form of therapy, but there is another group that does, and often in dramatic manner. The fundamental factors underlying this difference in response have not been determined as yet, and it is possible that further research in the direction of Dr. Rothman's work may lead to the solution of this important problem.

Attention should be called, however, to the occurrence of cases in which therapeutic failures would result from incidental treatment conditions. One of these conditions is lack of cooperation. I have records of patients with generalized, supposedly resistant infections who never got well until subjected to adequate treatment for a short period in the hospital under good nursing care. In some cases failure is the result of improper technique in the application of the ointment. This should be rubbed with some force, using a piece of towel if necessary, for two or three minutes, at least twice daily, over each infected area. A third factor often leading to failure is the occurrence of extensive dermatophytid reactions which naturally do not respond to the application of the ointment in situ. In cases showing such reactions, the actual foci of infection, which may be few and small, should be carefully located by laboratory examinations of skin scrapings from different regions, and treatment should be intensified on those locations. A fourth condition that may hinder the effect of treatment is the adaptation of the parasite to the therapeutic agent. I have seen this happen recently in a case of onychomycosis of three fingernails in which the patient discontinued therapy after the infection had been completely eradicated in two of the nails while the third still showed signs of disease. Resumption of treatment one month later failed to affect the infection thereafter. I feel that parasitic adaptation may be prevented by using the therapeutic agent in progressively intensive concentrations and without interruption until the maximum effect has been achieved.

Another important aspect of the therapeutic problem is the liability to recurrence. This appears to be dependent on at least two important factors, namely: host predisposition and latent residual foci of the fungus. As in any other infectious disease, there are certain persons who become easily and repeatedly infected; whereas others, who live under similar conditions, do not. Such a situation is not uncommon among married couples. The mechanism of individual susceptibility for this disease is not well understood, and there is practically nothing that can be done to cope with this phase of the problem.

The recognition of residual foci of the fungus after the skin has been cleared of infection is a most important factor in the treatment of this disease. Such latent foci, usually ignored by the patient, are to be found, as a rule, on the toes or toenails, and they serve as parasitic reservoirs from which infection may spread from time to time to other parts of the skin. Consequently, patients suffering from T. rubrum infections should never be discharged without a careful examination of the feet. The difficulties in the treatment of onychomycosis are fully recognized. However, with patience and proper technique a large proportion of the nail infections may be definitely eradicated. It should be borne in mind that the thick, infected nails must be destroyed as far as possible by mechanical means before resorting to fungicidal medication, and here the cooperation of the chiropodist may be of value. I have been very much impressed by Dr. Rothman's report on the effective action of lithium bromide as a keratolytic agent in these cases.

DR. MAURICE J. COSTELLO, New York: In the case cited by Dr. Lewis as mine, that with monocytic leukemia, the cutaneous eruption resembled granuloma fungoides, psoriasis, and lastly a generalized fungous infection. It did not resemble the generalized pruritic vesiculobullous eruption caused by T. rubrum which in so many instances is treated as dermatitis herpetiformis, because it resembles it clinically and because it is resistant to therapy.

Dr. Lewis, I am sure, will be the first to admit the possibility of coincidence or linkage of circumstances, but we shall have to admit that it would be very unusual for two rare diseases such as these to occur at the same time. All of the cutaneous lesions in my patient disappeared about two weeks before his death. Nodose lesions were seen on the face, arms, and legs. It is interesting to note here that the T. rubrum infection apparently followed rather than preceded the lymphoblastomatous disease. It is possible that the lymphoblastomatous disease changed the reaction of the skin, making it susceptible to fungous infection.

We do not see many cases of T. rubrum infections of generalized type in New York City, but I agree with Dr. Lewis that they are extremely refractory to treatment. The types that seem to respond well, or as well as Dr. Carrión suggested a moment ago, are the vesiculobullous types, those resembling dermatitis herpetiformis, even though they have been present for many years and oftentimes erroneously treated as Duhring's disease.

DR. HARRY L. ARNOLD JR., Honolulu, T. H.: I should like to recount for the record, apropos of Dr. Lewis' most interesting cases, a case seen some 15 years ago in Ann Arbor, Mich., of generalized discoid seborrheic dermatitis, in which Dr. Wile predicted the onset of leukemia some weeks or months in advance of the event. The diagnosis of seborrheic dermatitis was founded on clinical evidence only, and I suppose it is possible that it was erroneous and that we were in fact dealing with a T. rubrum infection. The patient had a normal blood cell count at the time Dr. Wiles prediction was made and returned to the hospital some weeks or months later moribund with acute monocytic leukemia.

DR. LOUIE H. WINER, Beverly Hills, Calif.: Drs. Thomas Sternberg and Josephine Tarbot recently showed me sections of nodes removed from the peritoneal cavity of mice which had been inoculated with T. rubrum. On staining these with hematoxylin and eosin, I was impressed by the similarity to Hodgkin's disease. However, the Hotchkiss-McManus stain readily disclosed the organisms, which were not evident in the hematoxylin and eosin stained slides.

DR. STEPHAN ROTHMAN, Chicago: I wish to thank the discussers for their remarks and suggestions. It is my experience that there are T. rubrum infections which can be easily controlled as infections with T. mentagrophytes. This is particularly true in cases of diabetics who happen to acquire this infection, mainly in intertriginous localization. However, the hyperkeratotic lesions on palms and soles as well as the nail infections are intractable for all practical purposes. The majority of persons with such lesions show a conspicuously flat glucose tolerance curve. Dr. Weidman's point is well taken. We should have used controls with T. mentagrophytes infection. However, such intractable hyperkeratotic T. mentagrophytes infections seem to be extremely rare.

Our hypothesis on adaptation originated with the work of F. M. Melton (*J. Invest. Dermat.* **17**:27, 1951), who demonstrated that filamentous fungi preferentially utilize carbohydrates, but when "starved" they learn to utilize nitrogenous materal. Grunberg and his associates (*Tr. New York Acad. Sc.* **13**:22, 1950) were the first to suspect that fungistatic agents act by interfering with the carbohydrate utilization of fungi.

Glucose promotes the growth of T. rubrum up to 4% concentration. Very high concentrations, from 20% up, however, inhibit growth, particularly if the strain previously was grown on a glucose-free medium.

Lithium bromide was chosen on the basis of the work of P. Alexander (*Ann. New York Acad. Sc.* **53**:655, 1951). He showed that lithium bromide loosens the structure of keratin by breaking hydrogen bonds.

I do not believe that in our material lack of cooperation on the part of the patients, as Dr. Carrión mentioned, was a decisive factor in the exasperating chronicity of the disease. The great majority of our patients were anxious to get cured and did everything they were told to do. Still, they did not get rid of their infection by any of the conventional fungistatic agents, in spite of trimming, filing, and evulsion of nails.

Dr. George M. Lewis, New York: A statement in the paper that generalized erythema due to T. rubrum is rarely seen in New York should not be misinterpreted. The usual foot, hand, and nail involvement is common in New York, as it is in most sections of the United States. Plaque-like manifestations over the buttocks, leg, or other areas also are not unusual. The present paper is concerned with those cases in which the disorder exhibits widespread dissemination of the disease. I appreciate Dr. Weidman's scholarly analysis of the data and his critical appraisal of our conclusions. In studying these patients, we felt the need for more definitive measures in order to prove or disprove the apparent association between infection and neoplasm. It would seem premature to speak with authority at this time. I am glad that Dr. Carrión has discussed the therapy of superficial fungous disease and has found benzoic and salicylic acid ointment still useful in comparison with the newer drugs and formulas. I would support him in this conclusion. It is to be hoped that Dr. Winer will report on his experimental work in animals, which would appear to be of great importance. Dr. Costello generously allowed me to include his case in the presentation, and I appreciate his help. Dr. Rothman has evolved a very ingenious theory, and it is to be hoped it will be just as he has it planned. There may be still time for lymphoblastoma to develop in his patients as months or years seem to mean little in the interval between onsets of these disorders.

AQUEOUS SOLUTIONS OF SODIUM PROPIONATE WITH CHLOROPHYLL AS A THERAPEUTIC AGENT

SAMUEL M. PECK, M.D.
EUGENE F. TRAUB, M.D.
AND
HERBERT J. SPOOR, M.D., Ph.D.
NEW YORK

FOR MANY years one of us (S. M. P.) has been using sodium propionate in an aqueous solution as a therapeutic agent.[1] Further experiences over the last few years have led us to believe that the use of this agent has proved helpful in many conditions in which wet dressings, vaginal douches, or mouth washes are indicated. While the sodium propionate solution was quite acceptable to most patients because of its beneficial effects, there was resistance to its continued use in some instances because of the odor problem associated with the application of the fatty acid salts. It was for this reason that we attempted to circumvent this objection by the addition of water-soluble chlorophyllin. This was a fortunate idea since the combination of the chlorophyllin and the sodium propionate for all practical purposes eliminated the odor problem. In addition, as has happened so many times in the course of research, an unexpected observation was made that the chlorophyllin not only acted as a deodorant but also seemed to enhance some of the therapeutic properties of the sodium propionate.

MATERIALS AND METHODS

For clinical application a powder was made in which there was 99.75% sodium propionate and 0.25% of a water-soluble chlorophyll derivative by weight, namely sodium copper chlorophyllin. The patients were instructed to dissolve the contents of an envelope (2.3 gm.) in a glass of water (6 oz., or 180 cc.), for use as a wet dressing or a mouth wash.[2] There resulted from this mixture approximately 1% of sodium propionate and 0.0025% of the chlorophyllin. In some instances, in which a stronger therapeutic concentration was required, two or even three envelopes of powder were dissolved in the same amount of water. In some instances, especially for foot baths, the 2.3 gm. of the chlorophyllin preparation was dissolved in a pint (473 cc.) of water.

From the Dermatologic Service of the New York Medical College.

1. Peck, S. M., and Rosenfeld, H.: The Effects of Hydrogen-Ion Concentration, Fatty Acids, and Vitamin C on the Growth of Fungi, J. Invest. Dermat. **1**:237 (Aug.) 1938. Peck S. M.; Rosenfeld, H.; Leifer, W., and Bierman, W.: Rôle of Sweat as a Fungicide: With Special Reference to Use of Constituents of Sweat in Therapy of Fungus Infections, Arch. Dermat. & Syph. **39**:126 (Jan.) 1939. Peck, S. M., and Russ, W. R.: Propionate-Caprylate Mixtures in the Treatment of Dermatomycoses, with Review of Fatty Acid Therapy in General, ibid. **56**:601 (Nov.) 1947.

2. Prophyllin,® supplied through the courtesy of Rystan Company, Inc.

Monilial vulvovaginitis has been seen more frequently mainly as a complication of "mycin" therapy. The chlorophyllin propionate was very useful here as a douche. When there were acute symptoms, it was recommended that one powder (2.3 gm.) to one pint be used at first, and the concentration was then increased as indicated for the control of the moniliasis. Here, too, unexpected observations were made which will be discussed subsequently. In a concentration of 2.3 gm. to a pint it made a pleasant soothing douche for general use.

CLINICAL DATA

We are reporting our clinical experience with the use of the sodium propionate-chlorophyllin mixture in well over 100 cases. In more than 500 cases over the years the sodium propionate solution alone has been used in treatment, but the present report is limited to those in which the chlorophyllin plus the sodium propionate was used.

Irritation and Sensitization.—No actual cases of sensitivity were noted in the series reported herewith. In the use of sodium propionate alone in the same concentration and for the same purposes since 1939 by one of us (S. M. P.), no actual sensitization to the sodium propionate had been noted. In a large series of reports on the use of water-soluble chlorophyllin as an ointment in 0.5% concentration, no actual sensitivity to the chlorophyllin itself has been reported.[3] Since the popular use of the water-soluble chlorophyllin in the last year or so, no instances of sensitization to this chemical have been noted by any of us.

Maceration incidental to the use of the sodium propionate-chlorophyllin mixture was noted, and was similar to that which would be seen occasionally following the too prolonged use of any wet dressing. It was noted mainly in our series in cases in which the wet dressing was prolonged deliberately for experimental purposes.

EXPERIMENTAL DATA

Both chlorophyllin and sodium propionate have some bacteriostatic and fungistatic properties. Bacteriocidal[4] and bacteriostatic properties are possessed by chlorophyllin solutions to a limited degree, and these activities as well as fungistatic effects have been reported for sodium propionate.[5]

3. (*a*) Gruskin, B.: Chlorophyll—Its Therapeutic Place in Acute and Suppurative Disease: Preliminary Report of Clinical Use and Rationale, Am. J. Surg. **49**:49 (July) 1940. (*b*) Goldberg, S. L.: The Use of Water Soluble Chlorophyll in Oral Sepsis: Experimental Study of 300 Cases, ibid. **62**:117 (Oct.) 1943. (*c*) Bowers, W. F.: Chlorophyll in Wound Healing and Suppurative Disease, ibid. **73**: 37 (Jan.) 1947. (*d*) Cady, J. B., and Morgan, W. S.: Treatment of Chronic Ulcers with Chlorophyll: Review of Series of 50 Cases, ibid. **75**:562 (April) 1948. (*e*) Moss, N. H.; Morrow, B. A.; Long, R. C., and Ravdin, I. S.: Effectiveness of Chloresium in Wound Healing and Deodorant Effects, Report of the Council on Pharmacy and Chemistry, J. A. M. A. **140**:1336 (Aug. 27) 1949. (*f*) Zeligman, I.: Topical Chlorophyll Therapy in the Dermatoses, J. Invest. Dermat. **13**:111 (Sept.) 1949. (*g*) Combes, F. C.; Zuckerman, R., and Kern, A. B.: Chlorophyll: Its Use in Topical Therapy, A. M. A. Arch. Dermat. & Syph., to be published. (*h*) Morgan, W. S.: Chlorophyll Therapy: Review of 114 Cases, Guthrie Clin. Bull. **16**:94 (Jan.) 1947.

4. Rapp, S. W.: Chlorophyll, Illinois Dent. J. **8**:405 (Oct.) 1949.

5. (*a*) Peck and others.[1] (*b*) Wyss, O.; Ludwig, B. J., and Joiner, R. R.: The Fungistatic and Fungicidal Action of Fatty Acids and Related Compounds, Arch. Biochem. **7**:415 (Sept.)

(*Footnote continued on next page*)

Experiment No. 1.—Various concentrations of the combination chlorophyllin-sodium propionate were compared directly by laboratory assay with comparable concentrations of the individual ingredients for their action against bacteria and fungi. In the initial bacteriological series the antibiotic assay organism, Staphylococcus aureus P-209, was used as the test organism. The media used were the standard nutrient agar and the thioglycollate assay agar. Comparative values in

TABLE 1.—*Chlorophyllin-Sodium Propionate Comparison*

Bacteriological Studies—Cup Plate Inhibition Zones—Streak Plate—Guiteras Cup Molds

Test Substance	Test Organisms and Media					
	Staph. aureus P-209		P. ovale		L. acidophilus	
	Thio. Agar, Mm.	Nutr. Agar, Mm.	Type I, Mm.	Type II, Mm.	332, Mm.	4357, Mm.
Chlorophyllin						
100% powder	27	33	..	..	..	..
1% aqueous	11	14	..	..	..	..
0.25% aqueous (eq. chlorophyllin-sodium propionate)	10	11	..	..	..	..
0.10%	p. i.*	13	10	12	9	9
0.015% (eq. 5% powder)	0	8	..	..	..	..
0.010%	0	14	9	14	11	12
0.0025% (eq. 1% powder)	0	12	..	..	..	..
0.0010%	0	14	0	14	11	12
0.0005% (eq. 0.2% powder)	0	0	..	..	..	..
0.00025% (eq. 0.1% powder)	0	0	..	..	..	..
Sodium propionate						
100% powder	20	12	..	..	..	..
5% aqueous	0	8	..	..	..	..
1%	0	8	..	..	..	..
0.2%	0	9	0	0	0	0
0.1%	0	8	0	0	0	0
Chlorophyllin-sodium propionate						
100%	25	16	..	..	..	..
5%	0	9	..	..	..	..
1%	0	9	..	..	..	..
0.2%	0	11	0	8	12	11
0.1%	0	12	0	12	15	17
Boric acid solution						
1.0% (Appr. 1 tbs./qt.)	0	0	..	..	..	..
Aluminum acetate solution (1-10 dil.)						
1.2%	0	0	..	..	..	..
Magnesium sulfate						
1.0% (appr. 1 tbs./qt.)	0	0	..	..	..	..

* p. i. = partial inhibition.

1945. (*c*) Keeney, E. L.: Fungistatic and Fungicidal Effect of Sodium Propionate on Common Pathogens, Bull. Johns Hopkins Hosp. **73**:379 (Nov.) 1943. (*d*) Keeney, E. L., and Broyles, E. N.: Sodium Propionate in the Treatment of Superficial Fungus Infections, ibid. **73**:479 (Dec.) 1943. (*e*) Keeney, E. L.; Ajello, L., and Lankford, E.: Studies on Common Pathogenic Fungi and on Actinomyces Bovis, ibid. **75**:377 (Dec.) 1944. (*f*) Sulzberger, M. B.; Shaw, H. C., and Kanof, A.: Evaluation of Measures for Use Against Common Fungus Infection of the Skin: Screening Tests by Means of Paired Comparison on Human Subjects, U. S. Nav. M. Bull. **45**:237 (Aug.) 1945. (*g*) Theodore, F. H.: Use of Propionates in Ophthalmology: A Preliminary Report, Arch. Ophth. **41**:83 (Jan.) 1949; (*h*) Use of Sodium Propionate in External Infections of the Eyes, J. A. M. A. **143**:226 (May 20) 1950; (*i*) Ocular-Oral Syndromes, Oral Surg. **5**:259 (March) 1952.

terms of inhibition zones are tabulated in Table 1. The powder used in the wet dressing contained approximately 1% sodium propionate and 0.0025% chlorophyllin. Also shown are the values obtained for other wet dressing materials in common use in their appropriate concentrations.

Comment: These results were obtained in duplicate at least. Within the biological error of the method, they are accurate. A reading of 8 mm. measures the diameter of the cup. Best results were obtained by the streak method of inoculation. When pour plates were used the results were consistently much lower. The activity of all these agents is on the surface and not through diffusion to any appreciable extent. All bacterial inhibitions were more readily demonstrated on streak plates than on pour plates, showing that the demonstration of this property demands the presence of air. In order to permit more accurate evaluation of the inhibition zones, our assay technique utilized the "Guiteras" cup assay mold rather than the usual cup assay cylinder. Against the Staphylococcus aureus, especially when

TABLE 2.—*Comparative Study—Bacteria and Fungi*

Test No.	Test Substance	Streak Plate Inhibition Zones in Millimeters						
		Staph.	Strep. β	Esch. coli	M. aud.	M. gypseum	T. viol.	C. albicans
1	Chlorophyllin powder 100%	12	14	13	0	Sl. inh.	0	0
2	Sodium propionate powder 100%	10	12	0	0	9	Sl. inh.	Inh.
3	Chlorophyllin-sodium propionate powder 100%	11	12	0	Sl. inh.	18	Sl. inh.	Inh.
4	Chlorophyllin-sol. 0.0125% (eq. 5% chlorophyllin-sodium propionate)	0	0	0	0	0	0	0
5	Sodium propionate 5% water sol.	0	0	0	Sl. inh.	14	0	Mod. inh.
6	Chlorophyllin-sodium propionate 5%	0	0	0	Inh.	0	0	Mod. inh.
7	Chlorophyllin sol. 1% (max. water sol.)	13	9	14	0	0	0	0
8	Sodium propionate 1%	0	0	0	9	0	0	Sl. inh.
9	Chlorophyllin-sodium propionate 1%	0	0	0	0	11	0	Sl. inh.
10	Chlorophyllin sol. 0.0025% (eq. 1% chlorophyllin-sodium propionate)	0	0	0	0	0	0	0

thioglycollate fortified media were used to offset bacterial inhibitory effects, none of the agents was really effective except in higher concentrations. Bacteriostatic effects of the agents in their lower concentrations are shown by the satisfactory inhibition zones obtained with the nonstimulating nutrient agar medium.

Experiment No. 2.—Using special media chosen for each organism the various preparations were employed against a series of organisms consisting of Pityrosporum ovale (two types), Lactobacillus acidophilus (two types), hemolytic Streptococcus, and Escherichia coli.

Mycological evaluation of the three test materials was made against Microsporum audouini, Microsporum gypseum, Trichophyton violaceum, and Candida albicans.

Comment: Table 2 shows the results of streak plate tests. The pour plates gave better bacterial growth, but the method of seeding did not seem to make much difference with the fungi. Chlorophyllin and chlorophyllin-sodium propionate were effective against the P. ovale and L. acidophilus in their more dilute concentrations. Only concentrated chlorophyllin was effective against the Esch. coli. All three agents were effective against the Staphylococcus in their higher concentrations.

Sodium propionate alone was effective against M. gypseum and T. violaceum and chlorophyllin alone slightly inhibitory toward T. gypseum. Sodium propionate alone was also quite effective against C. albicans. Chlorophyllin-sodium propionate was inhibitory to M. audouini, M. gypseum, T. violaceum, and C. albicans.

Experiment No. 3.—Staph. aureus P-209 was exposed to the test agents for varying periods of 5, 10, and 15 minutes, then grown out in broth. Tryptose phosphate and thioglycollate broth were used. The thioglycollate stimulates growth of partially inactivated organisms and therefore makes a more exacting test.

Comment: This same inhibitory or bacteriostatic property of chlorophyllin for Staph. aureus has been shown by the "time-inactivation" technique. Organisms were exposed to appropriate concentrations of the several agents for 5-, 10-, and 15-minute periods, then innoculi were incubated in tryptose-phosphate and in thioglycollate broth. Only the 1% chlorophyllin showed inhibitory properties. Growth in tryptose phosphate was completely inhibited, that in thioglycollate partially.

TABLE 3.—*Exposure Time Inactivations*

	Tryptose Phosphate	Thioglycollate
Chlorophyllin		
5 min	No growth	Some inhibition
1%–10 min	No growth	Some inhibition
15 min	No growth	Some inhibition
0.0125%	Growth and no inhibition in all tubes	
0.0025%	Growth and no inhibition in all tubes	
0.0005%	Growth and no inhibition in all tubes	
Sodium propionate		
5%	Growth and no inhibition in all tubes	
1%	Growth and no inhibition in all tubes	
0.2%	Growth and no inhibition in all tubes	
Chlorophyllin-sodium propionate		
5%	Growth and no inhibition in all tubes	
1%	Growth and no inhibition in all tubes	
0.2%	Growth and no inhibition in all tubes	

Again this shows bacteriostatic rather than bactericidal activity. Comparable bacteriostatic effect was not demonstrable by the time-inactivation technique for either sodium propionate or chlorophyllin-sodium propionate in concentrations up to 5%.

ANALYSIS OF CLINICAL MATERIAL

Acute Contact Dermatitis.—Forty patients with acute contact dermatitis were treated with chlorophyllin-sodium propionate wet dressings during the acute stages. These included mainly allergic contact dermatitis. Many of the patients had their manifestations on the face, especially around the eyes. In this series there were also included cases of dermatitis around the genitalia and on the hands, as well as on other parts of the body.

We believe that as a wet dressing the chlorophyllin-propionate mixture was the most efficient type of agent any of us have used for similar conditions. Especially striking was the marked antipruritic property of the chlorophyllin-sodium propionate mixture. It was especially useful in dermatitis on the face since inadvertent contact with the conjunctiva did not produce any irritation.

In all cases it seemed to us to be the wet dressing of choice, even where there was some secondary infection, especially when this was apparently caused by the Staphylococcus.

Atopic Eczema and Neurodermatitis.—Twelve patients with atopic eczema and neurodermatitis were treated with the chlorophyllin-sodium propionate wet dressing

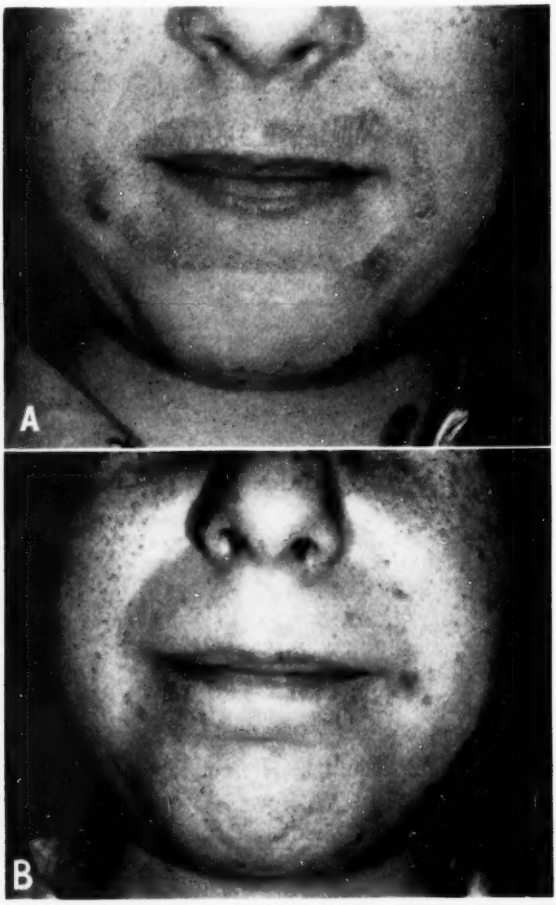

Fig. 1 (P. C.).—*A*, recurrent dermatitis around lips secondary to licking. Superimposed Monilia infection. *B*, beneficial result following use of chlorophyllin-sodium propionate as a mouth wash and a wet dressing.

during the acute stages. In some instances, definite irritation due to the previous therapy employed was present. The treatment was most useful during the acute stages and seemed to us to be soothing and nonirritating and especially helpful in allaying the itching. Once the acute symptoms had subsided, ointment therapy was resorted to.

Seborrheic Eczema.—Twelve patients with seborrheic eczema in the acute stage, with oozing and crusting, are included in this series. Most of the patients had their lesions around the ears, under the breasts (in women), in the groins, etc. There was a marked relief of the pruritus in all instances, with subsidence of the inflammatory manifestations. The chlorophyllin-sodium propionate mixture was especially useful in intertrigo.

It seemed to us that it was in the group of seborrheic eczema that we obtained our most striking results. The condition was improved in all the patients, and in

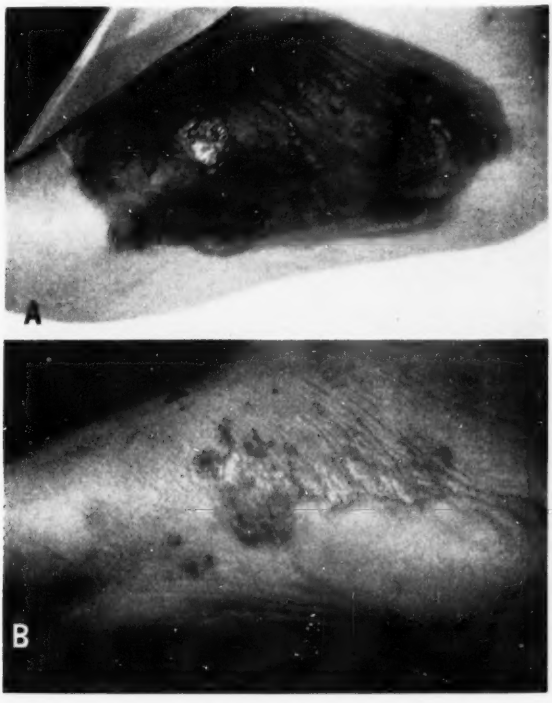

Fig. 2 (E. L.).—*A*, dermatophytosis of right foot, June 16, 1952. Discoloration due to gentian violet previously applied. *B*, improvement, Aug. 3, 1952, after use of foot baths twice daily with chlorophyllin-sodium propionate.

several it was almost entirely cleared up. This rather specific effect of sodium propionate in seborrheic eczema has been noted previously.

Rectal Eczema.—Six patients were treated, all females. The eczema was usually associated with vaginal itching and vaginal discharge. There was a marked relief of the itching during the application of the wet dressing. In one case it was used as a douche also. It was useful only in the acute stages of the dermatitis, especially for the relief of the pruritus. In no instance was the wet dressing alone sufficient to bring about a cure.

Dermatophytosis.—Fifteen patients with dermatophytosis of the feet, in most of them associated with hyperhidrosis, maceration, some secondary infection, and

cellulitis, were treated. The chlorophyllin-sodium propionate powder was used in a foot bath. Initially 2.3 gm. to a pint of water was prescribed twice daily, and in some instances the concentration was increased for a greater therapeutic effect. There was marked relief of the burning and itching, and the acute symptoms, especially the vesiculation and the cellulitis, were controlled. In most instances, as the acute symptoms subsided, a mild fungicide of the fatty acid type was used finally to bring about amelioration of the condition.

Oral Conditions.—In a concentration of 2.3 gm. to a glass of water, the chlorophyllin-sodium propionate mixture was very useful as a routine mouth wash. It was generally prescribed for use after each meal and upon retiring, and the full glass of the mouth wash was to be used. We are reporting a number of instances in which we have found that the mouth wash was especially useful.

Pemphigus with Manifestations in the Mouth: Three patients who had pemphigus with mouth manifestations are included in our series. The mouth wash appeared to be very soothing and seemed to keep the lesions much cleaner than they would have been if left alone. It was also useful in allaying the pain, and made eating much easier. However, as was to be expected, it did not influence the course of the lesions to any extent.

Aphthous Stomatitis: Four patients with aphthous stomatitis of the recurrent type were treated. The mouth wash relieved the pain and seemed to shorten the course of the condition.

Irritation from Dental Plates: In this condition the patient complained of soreness of the gums and of burning and redness of the palate where the plate was in contact. Six patients were treated. All had relief from the itching and burning.

Lichen Planus of the Mouth: Two patients with lichen planus of the mouth were treated for relief of the burning. Marked subjective relief followed the use of the mouth wash.

Leucoplakia: Two patients with leucoplakia on the mucosa of the cheeks and on the mucous surface of the lower lips were treated for relief of the associated burning. As in the cases of lichen planus of the mouth there was subjective relief but no clinical improvement.

Pustular Psoriasis.—Three patients with pustular psoriasis with manifestations on the hands and feet are included in this series. There was no effect on the clinical course of this condition after weeks of treatment.

Pemphigus with Manifestations in the Groin.—One patient who had pemphigus with extensive lesions on the body generally, but especially in the inguinal regions, were treated with the wet dressings. The applications seemed to have a markedly soothing effect, and they tended to reduce the secondary infection.

Reactions Following the Use of Antibiotics.—There were seven patients with vulvovaginitis due to Monilia. The chlorophyllin-sodium propionate mixture was used as a douche and as a wet dressing. The pruritus was greatly relieved, and the discharge seemed to be beneficially influenced. Most of the patients used the chlorophyllin-sodium propionate solution for at least five weeks and continued its use as a douche for a long time thereafter. The concentration of the solution was increased from one to two powders to a pint in a number of instances with beneficial results. In most instances, to bring about a cure a preparation such as propi-

onate compound jelly (propion® gel) had to be used with the douche. It was most striking to note the immediate relief of the itching following the use of both the douche and the wet dressing.

Three patients with rectal and scrotal dermatitis following the use of penicillin and aureomycin were also treated. Marked relief of acute manifestations was obtained with especially beneficial effects on the course of the pruritus.

There was one especially noteworthy case of acute vesicular dermatitis around the eyes following the use of an oxytetracyline ("terramycin") ophthalmic ointment. The condition showed decided improvement, with complete disappearance of symptoms. The chlorophyllin-sodium propionate wet dressing was especially useful here since contact with the conjunctiva did not cause any irritation.

Fig. 3 (A. L.).—*A*, furuncle on dorsum of finger, June 5, 1952. *B*, improvement after continuous wet dressings with chlorophyllin-sodium propionate, June 7, 1952.

Nummular Eczema.—Two patients with nummular eczema of the hands and forearm were treated. There was no improvement of the clinical manifestations.

Psoriasis.—Four patients with rectal-vaginal psoriasis were treated. The itching was reduced and some of the irritation seemed to be allayed, but there was no effect on the course of the condition.

Two male patients who had psoriasis with secondary irritation following the use of ointment were treated. There was a marked relief of the secondary dermatitis, and the wet dressing had a soothing effect and decreased the pruritus.

One patient used the wet dressing for over a year whenever the itching became too severe and reported that there was a marked relief in most instances during the application of the wet dressing and for several hours thereafter.

Burns.—Four patients with first- and second-degree burns on the face, hands, and forearms were treated. The wet dressing was very soothing and brought about healing in all instances.

Senile Pruritus.—Four patients with senile pruritus, all men, were included in the series. They presented the typical manifestations of dry scaly skin, especially on the lower extremities. In some instances excoriations were present. The regular concentration of one powder to a glass of water was used, but instead of a wet dressing the patients were instructed to rub the solution on the affected areas three or four times a day and allow it to dry. There was marked relief of the pruritus and the dryness in nearly all instances.

Varicose Eczema.—Twelve patients with dermatitis of the lower extremities on the basis of varicosities were treated. In four instances the varicosities were associ-

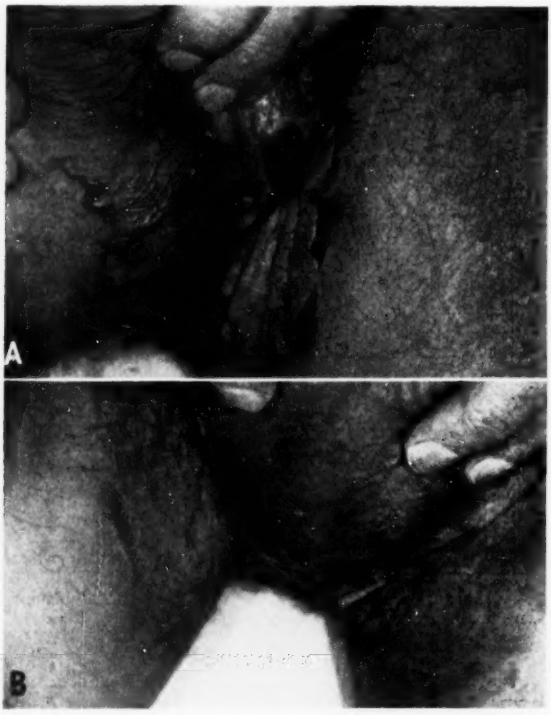

Fig. 4 (H. K.).—*A*, pemphigus vulgaris with lesions in groin, June 13, 1952. *B*, wet dressings with chlorophyllin-sodium propionate allayed itching and were soothing, June 25, 1952.

ated with ulcers. The wet dressings were useful when dermatitis was present. Where there was mild secondary infection of the ulcers, the ulcers became cleaner, and the infection seemed to be reduced. However, in all instances other therapy had to be used to influence the ulcer as far as healing was concerned.

Ichthyosis.—Two patients with ichthyosis were treated. The results here were very interesting. The standard solution of one powder to a glass of water was used, and the patients were instructed to rub the solution on the skin three or four times a day. One of the patients, a man, also used this solution as shaving water for more than one year. As long as the solution was used in this way the patients

seemed to acquire an artificial sweat; the scaling was reduced, and they felt much more comfortable. Clinically they were quite improved.

Moderate Secondary Infection.—A number of patients with moderate secondary infection were treated with the wet dressing. Included were trophic ulcers and diabetic ulcers of the toes, secondary infections associated with insect bites, etc. The acute symptoms were relieved, and in some instances the infection was completely controlled. However, when the infection was more severe other therapy had to be used to bring about complete cure.

Acute and Chronic Paronychia.—Ten patients with acute and chronic paronychia were treated with the wet dressing. In cases in which the paronychia was

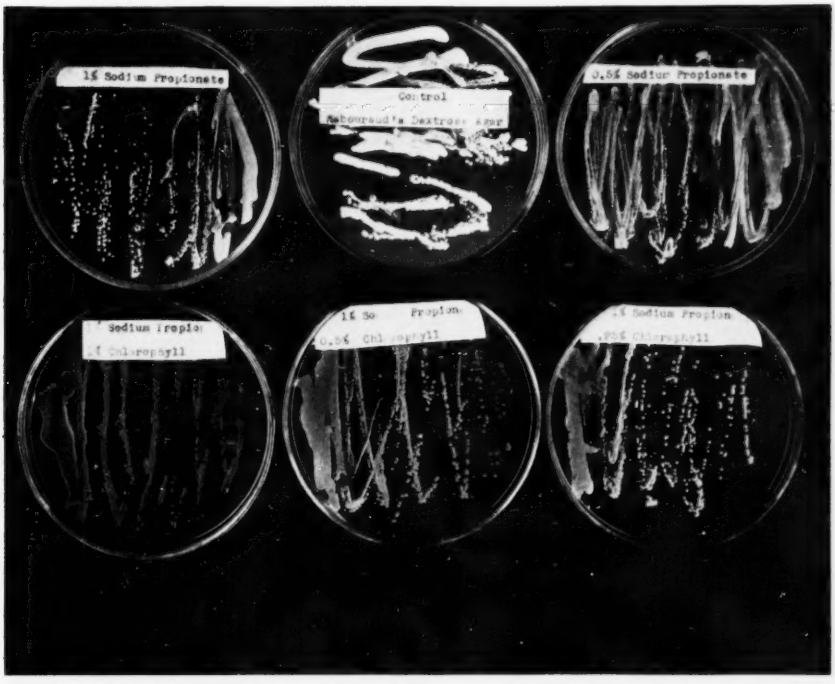

Fig. 5.—Fungistatic effect of sodium propionate on C. albicans; 48-hour growth on Sabouraud's dextrose agar; antifungal agent dispersed through medium as indicated.

situated around the base of the toenails, foot baths were prescribed. The acute inflammation was beneficially influenced, but there was no effect on the course of the chronic paronychia.

Small Operative Wounds.—In a number of instances after the removal of moles, warts, etc., the chlorophyllin-sodium propionate powder, full strength, was dusted directly on the wounds to make an artificial crust. There was satisfactory healing under such a crust.

Herpes Simplex.—A number of cases of herpes simplex around the mouth and around the genitalia were included in our series. Wet dressings for 7 to 10 days were found to be soothing and seemed to favorably influence the course of the eruption.

Exudative Discoid and Lichenoid Chronic Dermatitis.—Two patients with "oidoid" disease were treated, similarly to those with senile pruritus and ichthyosis. There was no effect either objectively or subjectively.

Duhring's Disease.—Five patients with Duhring's disease were treated with the wet dressing. Where there were manifestations of more eczematoid type the patients were instructed to apply the solution directly three or four times a day. Although the itching was relieved, there was no effect on the clinical course of any individual patch of this disease.

Diaper Rash.—Recently it was noted in a small series of cases that the combination of chlorophyllin-sodium propionate as a wet dressing and the use of an oint-

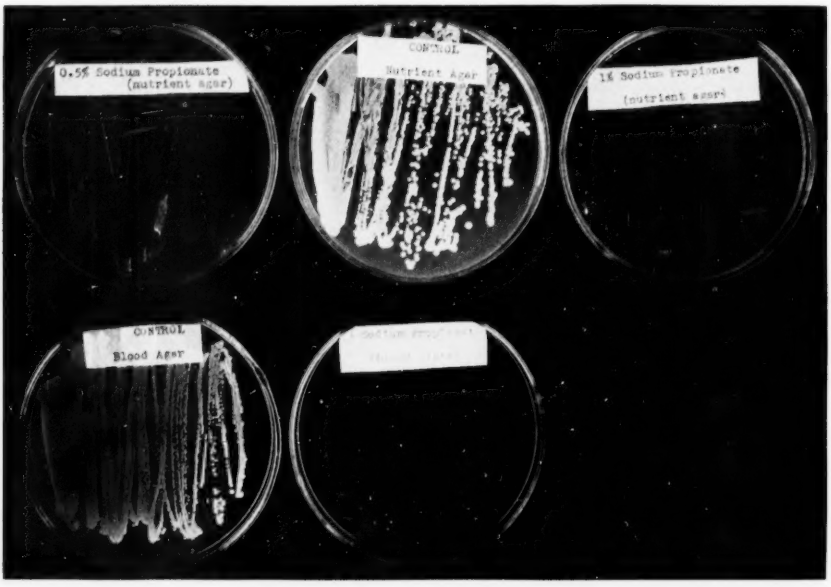

Fig. 6.—Bacteriostatic effect of sodium propionate on Staph. aureus; 48-hour growth on nutrient or blood agar as indicated; antibacterial agent dispersed through medium as indicated.

ment containing 5% sodium propionate and 0.0125% chlorophyllin seemed to be an effective treatment for diaper rash. The wet dressing quickly controlled the acute symptoms, while the ointment acted as a healing and protective application and helped prevent recurrences. Disagreeable odors were quickly reduced or eliminated.

GENERAL COMMENT

In recommending a new type of wet dressing, it is not intended to imply that we are introducing a curative preparation, except for a few acute conditions. The sound basis for the use of a wet dressing is well established and needs no elaboration here. It is usually given for the symptomatic relief of certain stages of a dermatitis or to favorably influence the course of an infection.

We believe that the use of the chlorophyllin-sodium propionate mixture introduces a marked advance in wet dressing therapy because it has the following advantages:

(*a*) It is more nearly physiologic in its action.

(*b*) It is nontoxic.

(*c*) It is bacteriostatic and fungistatic.

(*d*) It seems to promote healing, which may be due partly to the chlorophyllin content.

(*e*) It has especially marked antipruritic and soothing properties.

(*f*) It has a low index of sensitization.

The addition of the chlorophyllin, even in the low concentration in which it was used, seems to enhance the antipruritic action of the fatty acids. This antipruritic property of sodium propionate has been noted previously by many observers who were using the fatty acid preparations in the treatment of various types of mycosis. In some instances in proper concentration sodium propionate can be said to have an almost local anesthetic effect.

There have been increasing indications that there is a possibility of boric acid poisoning by transcutaneous absorption through the broken skin. Sodium propionate is nontoxic in relatively large doses. For years it has been incorporated in bread and cake to prevent molding. One of us (S. M. P.) has treated a large series of patients by the intramuscular administration of 2 to 5 cc. of 5% sodium propionate for months without any evidence of toxic effects. Animal experiments in which the sodium propionate was given intramuscularly and intraperitoneally also demonstrated that it was of low toxicity.

Chlorophyllin in various concentrations has been used in the treatment of burns, wounds, and ulcers, as well as over large areas of dermatitis, without any ill effects.[3] In animal experiments, it has been administered intravenously and intramuscularly in amounts far exceeding that which could possibly be absorbed through the skin and mucous membranes, with no deleterious effects.[6]

Peck and his group,[1] as well as Keeney and others[5c-e] have demonstrated the fungistatic and fungicidal properties of sodium propionate and other fatty acids. Such effects are further illustrated by the experimental data included in this report.

T. G. Anderson, in a personal communication, reports that in a series of 43 strains of freshly isolated C. albicans all were sensitive in vitro to sodium propionate. The work of Keeney as well as the data which we are presenting substantiates this finding.

Theodore[5g-i] has used sodium propionate on about 1,200 patients with infections of the lids, conjunctiva, and cornea. He reports results which compared favorably with those noted with the antibiotics. Theodore,[5g] working in Peck's laboratory, reported inhibiting effects of sodium propionate against Staph. aureus, Staph. albus, hemolytic streptococci, streptococci of the viridans group, pneumococci, Esch. coli, Bacillus subtilis, and Bacillus enteridis. The effect against Pseudomonas aeruginosa (Bacillus pyocyaneus) is of special practical importance.

6. Smith, L. W.: Chlorophyll: An Experimental Study of Its Water-Soluble Derivatives; Remarks upon the History, Chemistry, Toxicity, and Antibacterial Properties of Water-Soluble Chlorophyll Derivatives as Therapeutic Agents, Am. J. M. Sc. **207**:647 (May) 1944.

Keeney and his associates [5c] demonstrated that propionates were superior in vitro in their antibacterial effects on Staph. aureus and beta hemolytic Streptococcus to sulfathiazole. Our experiments have shown similar bacteriostatic properties for the sodium propionate.

The water-soluble fraction of chlorophyll has been shown by a number of observers [7b-d] to have an accelerating effect on wound healing.

The low toxicity and low sensitizing properties of the chlorophyllin have been reported by many authors in both clinical and animal experiments.[3]

The bacteriostatic activity of water-soluble chlorophyll has been noted by Morgan [3b] and Rapp [4] as well as in the report of the Council on Pharmacy of the American Medical Association in 1949.[3c] Our findings also indicate that chlorophyll (water-soluble) has bacteriostatic but no bactericidal effects, at least under our experimental conditions.

A great many dermatologic conditions have been treated over the years with water-soluble chlorophyll both in ointments and in solutions.[7a-d] The results in burns, wounds, and ulcers were especially noteworthy. The reports stress the lack of irritation and the marked soothing and healing properties. We have been most favorably impressed by the clinical improvement of roentgen dermatitis with chlorophyllin ointment. In our experience it gave better results than any other form of therapy.

In comparison with boric acid the sodium propionate chlorophyllin solution is much less toxic. It is also much more bacteriostatic and fungistatic and seems to promote healing.

The astringent action of aluminum acetate (Burow's) solution is undesirable in many cases. The studies of Sulzberger and his group,[8] as well as those of Shelley and his co-workers,[9] have shown that in many instances a miliaria-like component is an important factor in some dermatoses. It is this factor which may play a role in excessive pruritus accompanying such conditions. In this regard the chlorophyllin-sodium propionate wet dressing is comparable to isotonic sodium chloride solution. It can be seen from our laboratory studies that the chlorophyllin-sodium propionate solution is bacteriostatic and fungistatic while aluminum acetate solution is not.

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7. (*a*) Goldberg. [3b] (*b*) Lowry, K. F., and Curtis, G. M.: Pertinent Factors Influencing Repair in Traumatic Wounds, Am. J. Surg. **78**:781 (Nov.) 1949. (*c*) Smith, L. W., and Livingston, A. F.: Chlorophyll: An Experimental Study of Its Water Soluble Derivatives in Wound Healing, ibid. **62**:358 (Dec.) 1943. (*d*) Collings, G. H., Jr.: Chlorophyll and Adrenal Cortical Extract in the Local Treatment of Burns, ibid. **70**:58 (Oct.) 1945.

8. Sulzberger, M. B.; Zimmerman, H. H., and Emerson, K., Jr.: Tropical Anhidrotic Asthenia (Thermogenic Anhidrosis) and Its Relationship to Prickly Heat, J. Invest. Dermat. **7**:153 (Aug.) 1946. Sulzberger, M. B.; Zak, F. G., and Hermann, F.: Studies of Sweating: II. On the Mechanism of Action of Local Antiperspirants, Arch. Dermat. & Syph. **60**:404 (Sept.) 1949. Sulzberger, M. B.; Hermann, F.; Keller, R., and Pisha, B. V.: Studies of Sweating: III. Experimental Factors Influencing the Function of the Sweat Ducts (A Preliminary Report), J. Invest. Dermat. **14**:91 (Feb.) 1950.

9. Shelley, W. B.; Horvath, P. N.; Weidman, F. D., and Pillsbury, D. M.: Experimental Miliaria in Man: I. Production of Sweat Retention Anidrosis and Vesicles by Means of Iontophoresis, J. Invest. Dermat. **11**:275 (Oct.) 1948. Shelley, W. B., and Horvath, P. N.: Experimental Miliaria in Man: III. Production of Miliaria Rubra (Prickly Heat), ibid. **14**:193 (March) 1950.

The use of solutions of antibiotics for specific purposes cannot be compared to the fatty acid-chlorophyll mixture since the bactericidal and bactériostatic effects of the former are far greater than those of the wet dressings we are discussing. However, in our work we have supplemented the internal use of an antibiotic with the external application of the chlorophyllin-sodium propionate wet dressing as a combined method to be used when necessary, since the tendency to sensitization to the antibiotic, as is well known, is much greater on external application than after internal administration.

Other wet dressings, such as Alibour water and silver nitrate, while they may be bacteriostatic under certain conditions, seem to us to be not much better in their actions than the chlorophyll-fatty acid solution and have the additional minus of staining the skin.

The physician is often at a loss to prescribe a routine vaginal douche that will not interfere with the action of medication introduced into the vagina. We have found that the chlorophyllin-sodium propionate solution makes an ideal vaginal douche for ordinary hygienic purposes, and in addition is especially to be recommended because of its bacteriostatic and fungistatic effect, especially on C. albicans.

The mouth wash has been used extensively for many conditions in which a soothing, mildly antiseptic action is required. It has also been used routinely by us for symptomatic therapy, such as the relief of an ordinary sore throat. It has proved very useful as a refreshing mouth wash for ordinary oral hygiene.

In addition to its routine use as a foot bath as part of the treatment of dermatophytosis, it was useful to control hyperhidrosis and maceration, often associated with fungus infection on the feet. Many of our patients have continued the use of such foot baths long after the manifestations of the dermatophytosis have been controlled because of the beneficial action of the chlorophyllin-sodium propionate mixture on hyperhidrosis.

SUMMARY AND CONCLUSIONS

Experimental and clinical studies of sodium propionate with chlorophyllin as a therapeutic agent have been reported.

It has been used as a wet dressing, mouth wash, vaginal douche, and foot bath in well over 100 cases.

It seems to be particularly useful because of its (*a*) more physiologic action; (*b*) lack of toxicity; (*c*) low sensitizing index; (*d*) bacteriostatic and fungistatic properties, and (*e*) soothing, healing, and especially antipruritic effects.

MECHANICAL TRAUMA

A Study of Its Role in a Group of Skin Diseases Reputedly Influenced by Trauma

ALBERT R. McFARLAND, M.D.
ROCHESTER, N. Y.

IN VIEW of the popularity of the subject of psychosomatic trauma in medicine in recent years, I have felt the urge to evaluate the other side, namely, mechanical trauma in certain skin diseases. This review includes an instance in which trauma is solely, partially, or questionably an etiological factor, and some suggestions regarding the prevention and modification of trauma.

The first class of diseases consists of those in which trauma, by universal agreement or definition, is the sole cause. These diseases may be divided into four groups.

Group 1 includes thickening and hyperpigmentation of traumatized areas, such as elbows, knees, and buttocks, produced by pressure and friction. These conditions need only be mentioned in passing, and are easily corrected by occupational adjustments, correction of mannerisms, or a cushion on a chair.

Group 2 are the factitious dermatoses. These fall into two general subdivisions. The first includes malingering, in which some form of trauma is applied by a facetious patient in an attempt to puzzle his physician, excite sympathy, or collect a compensation claim. A frank exposure of the trickery may be sufficient. In the second there exists a major or a minor psychoneurosis, but not malingering. In this group are trichotillomania, habit rubbing of the hair, biting of nails and cuticle, and "pick acne" in which the acne is minor and the inferiority complex is major. Often a friendly talk by the physician is sufficient. However, the element of trauma may be overlooked, and this may lead to an erroneous diagnosis and unnecessary treatment.

Group 3 consists of the more bothersome and deep-seated psychoses manifested in neurotic excoriations and acarophobia. Neurotic excoriations is a diagnosis which I am inclined to make less frequently, as a result of a summary of my case histories in this group. All too frequently in cases in which that was my original diagnosis, I find that later revised diagnoses included pyoderma, which responded to antibiotics, papulonecrotic tuberculid, and atypical dermatitis herpetiformis; and, I blush with shame to note, one case which turned out to be pediculosis corporis.

The cases of acarophobia follow a distinct pattern. I have recorded nine true cases in the past five years. All patients were sure something was crawling on their skins. Most of them had with them an envelope containing a few dried scales which they were convinced jumped and moved. My failure to observe the jumping dis-

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turbed them greatly. A placebo usually cured them for about two weeks. Most of these cases were referred to the psychiatrists, but I have yet to see any permanent help from that source.

In Group 4 are calluses and corns. The ordinary calluses of the palms are no problem, and are of course a very real protection to the laborer. They disappear when friction is stopped. Calluses on the feet, however, are a different problem. People must walk and stand on their feet, and the ensuing discomfort may be almost crippling. Soaking, paring, and salicylic acid preparations may help some, but at best are not very satisfactory. I have been much interested in these persons with multiple painful calluses and corns over points of pressure. During the past few years I have resorted to only one simple method of therapy, namely, to prescribe shoes with thick foam-rubber soles. Such shoes are clumsy-looking, and women sometimes rebel; but in men cooperation is easy, and the relief obtained is very gratifying. I have records of 16 cases which have been followed for one or more years. It takes at least three months to obtain noticeable relief, but after six months the improvement of these feet is really amazing. I recommend it for your trial. Insoles do not seem to be sufficient, and to obtain results this type of shoe must be worn constantly.

The second major classification consists of those diseases in which trauma is the trigger factor that initiates symptoms in an underlying abnormal physiology. Persons who bruise easily and are constantly covered with black and blue marks usually have a vascular fragility which can be helped by long-continued dosage with rutin, 20 mg. three times a day. Improvement may be judged by the tourniquet test. Dermographism is elicited by trauma. The nature of the underlying instability is uncertain, but I believe that nervous tension and irritability play a part. I could locate the records of only four cases of epidermolysis bullosa, but in all of them the well-recognized role of trauma seemed to be present. The predisposition is probably a hereditary defect. Paronychia is in the last analysis a bacterial infection, but in over 90% of our cases there was a definite history of trauma either from manicuring or from housework, such as scrubbing or hand laundry. In varicose ulcers I found that trauma was almost always an initiating factor, but the underlying disease is, of course, venous stasis and is best treated by surgery. As an alternative, supporting bandages, or zinc oxide paste (Unna) boots are palliative.

The third major classification includes cancers and precancerous lesions in which traditionally trauma has been blamed for so long that it is almost accepted as axiomatic. One such condition is leucoplakia. It seems to me that this hypothesis is not tenable. In 46 cases reviewed only 14% of the lesions were so situated as to be grossly exposed to trauma, as at the dental occlusion line or opposite a jagged tooth. More often the leucoplakia lesions were high up in the labial-dental fold, on the palate, back of molar teeth, or diffusely scattered over the oral cavity without relation to points of trauma. Leucoplakia of the vulva was found in unpredictable areas. It seems more tenable that leucoplakia is a degenerative process of unknown origin and that trauma plays only a minor part.

Also senile and seborrheic keratoses were found to have no consistent relation to trauma in their location.

Regarding cutaneous cancers, my case histories seem to throw considerable doubt on the role of trauma. I selected at random 100 cases of all types of skin

cancer and found that in only 23% could trauma be seriously considered, even by giving it the benefit of doubt whenever possible. To mention only a few of the common sites, lesions were located high on the cheeks, back of the ears away from bows of glasses, on the margin of the ears, tip of the nose, upper lip, sides of the neck, between the shoulders, and on the backs of the hands. Some of these areas may be subject to irritation from sun, wind, and actinic rays, but are not particularly subject to trauma. On the other hand, areas such as the soles, palms, elbows, knees, buttocks, and perianal regions, which are constantly subjected to trauma, were almost never affected. I am well aware of the evidence on the other side and even of the occasionally reported cases in which a single trauma has preceded cancer, as in a recent paper by Downing,[1] but percentage-wise, in my experience, this is not impressive.

The fourth classification consists of those diseases in which trauma is an aggravating or continuing factor in an otherwise well-established clinical entity. This was found to be true in cases of lichen planus and psoriasis in which new lesions sometimes developed at the site of a scratch mark or bruise. Scratching also consistently aggravates almost any itchy skin disease, such as atopic eczema, infantile eczema, and dermatitis herpetiformis.

I should like to comment particularly upon the entity of localized patchy lichen simplex or neurodermatitis with reference to a mode of treatment used. Over the past few years I have used a protective covering to prevent trauma from scratching, with gratifying results. It is true that many patients respond to conventional methods, such as treatment with x-ray, ultraviolet light, salicylic acid preparations, iodochlorhydroxyquin (vioform®), and even such drastic measures as applications of potassium hydroxide, silver nitrate, or trichloroacetic acid, as advocated by Sidi.[2] However, many patients do not respond to these methods. Their treatment consisted of applying a layer of zinc oxide (Lassar's) paste, then a gauze covering, and over this a well-fitting elastoplast® bandage. These dressings are left on for two to three weeks. Upon removal of the dressing, the area is somewhat macerated but less lichenified and less inflamed. Relief from itching is striking. The dressing is changed about once in two weeks until the skin returns to normal. Probably the benefit is due to mechanically preventing the patient from scratching. This method should not be used where there is obvious secondary infection or where weeping exists. It is of course only applicable to areas which lend themselves to bandaging. I have collected the histories of 56 patients over the past four years who have been treated by this method and who have been followed long enough for the observations to be of value.

It did not seem practical to classify the results on a percentage basis, as the degree of relief varied and recurrences sometimes took place. However, the general impression, from progress notes, is that nearly all received some degree of relief, and a great many seemed to have complete cures. I find that I am resorting to this method of treatment more and more as time goes on. This procedure is, of course, not new or original, but perhaps it is used too infrequently. In my series of cases it proved to give gratifying results.

1. Downing, J. G.: Cancer of the Skin and Occupational Trauma, J. A. M. A. **148**:245 (Jan. 26) 1952.

2. Sidi, E.; Goetschel, G. E., and Casalis, F.: Trichloroacetic Acid in Dermatoses, Presse méd. **58**:570 (May 20) 1950.

SUMMARY AND CONCLUSIONS

The role of trauma in a group of skin diseases has been studied. It is concluded that trauma may be a sole cause or a contributing and modifying factor. It may be inflicted deliberately, unintentionally, or unavoidably. Statistical studies of each group are recorded.

Trauma from scratching may be eliminated under some circumstances by mechanical protection, as described.

Trauma from pressure or friction may be helped by change of habits, occupation, or protective devices.

The role of trauma in initiating or aggravating leucoplakia, cancers, and precancerous lesions is thought to be questionable.

ABSTRACT OF DISCUSSION

DR. HOWARD J. PARKHURST, Toledo, Ohio: This paper is of considerable practical importance. I agree that a diagnosis of acarophobia should be made only if a patient complains of parasites digging into the skin and not merely of a burrowing sensation. I agree that such cases are not often encountered, and I have had some good results by ordering a placebo which I claimed to be a "sure cure," and emphasizing the sureness of the cure. Regarding the subject of corns and calluses, I have always felt that really comfortable shoes were beneficial, being less productive of trauma, and I agree that those with foam-rubber soles are the most comfortable of all. The subject of oral leucoplakia calls for considerable discussion. I have seen fewer cases of leucoplakia in recent years and have felt that this diminution was probably due to generally improved oral hygiene and less chewing of tobacco and cigars. Most persons with ragged teeth and ill-fitting dentures do not acquire leucoplakia, and weak galvanic currents from dissimilar fillings do not often produce it. Some unknown predisposing factor is apparently needed. I agree that mechanical trauma usually plays little or no part in the growth of keratoses and epitheliomas, with the single exception of the jet-black mole. We all realize that even when irritated such moles usually do not becomes cancerous, but I should prefer not to take a chance with undue trauma. Occlusive dressings are effective in pruritic dermatoses, but they cannot be used in some locations. I always advise the use of thick cotton gloves or mittens, and the results have been very good. Obviously, it is also important to prevent excoriation in occupational dermatoses and in fungous infections.

DR. STEPHEN ROTHMAN, Chicago: It has been rather surprising to hear that statistically the role of mechanical trauma in the development of cutaneous cancers is not impressive. Experiments in my laboratory have shown that periodically repeated rubbing of the skin leads to measurable thickening of the horny layer (Rubin, L.: *J. Invest. Dermat.* **13**:313, 1949). Whereas the normal horny layer regulates its own thickness by continuous shedding, after mechanical irritation this shedding process is disturbed, more adherent and harder horny lamellae are formed, and hyperkeratosis results. This is the mechanism of callus and corn formation. The keratin of the horny layer becomes more similar to the nonshedding keratin structures, such as hair and nails. One may say that the horny layer undergoes a "superkeratinization."

There can be little doubt that in the early phases of keratoses and leucoplakias something very similar happens. The mechanical factor in the development of leucoplakias is often quite obvious, particularly in cases of ill-fitting dentures and bridges. I saw many "collar-button carcinomas" in Europe, where people wear narrow collars and the sharp edge of the collar button chronically irritates the skin above the thyroid cartilage.

I was very much interested to hear that Dr. McFarland was able to keep lichen Vidal patches under occlusive dressings. I never was able to persuade my patients to keep on such dressings because of the intolerable itching which always set in when the dressing was not changed.

DR. SAMUEL AYRES JR., Los Angeles: I think Dr. McFarland brought out some very interesting points, and we perhaps do not pay enough attention to trauma. I should like to make one comment with reference to acarophobia, or, as it is sometimes called, delusions of parasi-

tosis, and to disagree just a little with the prognosis in these cases. I think sometimes we give up a little too easily. I hate just as much as anybody else does to see such people come in with an envelope of "specimens" five minutes before lunch time. You have to allow ample time to go into such problems.

I think in most instances it will be found that these patients have some tangible disturbance, such as dryness from excessive bathing or possibly a metabolic disorder, which produces a paresthesia, a feeling of crawling, which they then misinterpret in terms of parasites. I roughly divide these patients into two classes—those who are recently afflicted and those who are confirmed in their delusions. The latter group I don't think are amenable to treatment except by a psychiatrist. In the former group, those who have had their "parasites" only for a matter of weeks or several months, I think the prognosis is not too bad. It has been my practice to take a very detailed history and give the patient plenty of time to discuss his problem, and then to take a very firm attitude with him. I don't agree with the idea of giving the patients a remedy and telling them it will cure their parasites. Such a procedure only strengthens their delusions. Most of them have already been to doctors who have given them something to cure their parasites, and they report, "Dr. So and So said I had parasites." I don't think you will cure them that way.

A patient who has only recently acquired this condition must be started right at the very first visit. After listening courteously and taking a good detailed history to bring out any possible local or constitutional factors, you should lay down the law to him very sternly and let it be known that if he wants help, and presumably that is why he came to you, the only way he can get it is just to relax a little and let you drive the engine a while. It may take several sessions before you will begin to get the idea across, but I have at least two or three patients who came to me with these envelopes full of so-called specimens, and who had been through many hands, and had got their skin irritated from strong medication, and in whom completely satisfactory results were obtained. Such a patient was in the other day and is completely healed. She was in for some other problem entirely, an epithelioma.

I think you can get good results if you take the firm attitude that you are the boss, and that if they expect to benefit, they have to do as you say. If they are confirmed in their convictions, they won't come back. If they want to get well, they will come back, and you can help them, and you may discover they have high blood sugar, anemia, disturbed liver function, or some other metabolic disorder. Very often these people are elderly, and they eat erratically and quite often are poorly nourished or may be suffering from hormone deficiencies of old age.

With reference to the calluses on the feet I was interested to hear about the sponge-rubber soles, and I am going to try that. But another therapeutic approach, particularly for the single large callus or callus-containing wart, is correction of the weight-bearing by an orthopedic surgeon, who may prescribe a metatarsal bar on the sole of the shoe. Trauma may precipitate a skin lesion by lowering the resistance to a latent infection already present, as in the development of a gumma after trauma. Another example is that of a patient who had a Trichophyton rubrum (purpureum) infection of the feet and one hand. He went to a football game, where an enthusiastic rooter hit him over the ear with a folded newspaper. After this a T. rubrum infection of the external ear developed. The trauma, by lowering local resistance, apparently allowed the fungus, which was present elsewhere on the body, to establish itself in the traumatized area.

Dr. Fred D. Weidman, Philadelphia: Dr. McFarland has listed numerous examples of mechanical factors which produce dermatoses. Naturally, others can be added. I thought of the cases of malocclusion which Dr. Martin Van Studdiford will discuss and the cases of granuloma fissuratum which the Suttons have brought to our attention. I want to add two other types of lesions which are not generally known, occurring in "wolf-biters" and "tail-chewers."

As to wolf-biters, this designation was given by Dr. Thomas Butterworth, who is consultant to a state institution for the feeble-minded. There he found that many of the inmates chew their knuckles. However, there are many people who lead monotonous lives and do not live in institutions. I recall that at one of our Philadelphia Dermatological Society meetings Dr. Butterworth suggested that diagnosis for a patient who was not an inmate of an institution. I do not know whether wolf-biting is related to knuckle pads or not, but it is a point that should be checked in future cases. That is, do some of the cases of knuckle pads occur in what Dr. Butterworth calls wolf-biters?

As to the tail-chewers, they are monkeys. As the result of the monotonous life which they lead, they chew away until sometimes only 5 or 6 in. of the tail are left. In fact, the monkey may become disfigured to the extent that he is unfit for exhibition and with an appendage of that sort has to be killed.

DR. FRANCIS A. ELLIS, Baltimore: I enjoyed this paper very much and want to discuss one phase of it. Since reading an article published on the treatment of burns with "Zinax" (*J. A. M. A.* **147**:741 [Oct. 20] 1951), I have been using "Zinax" (a partially hydrolized casein gel) dressing for stasis and pruritic dermatoses, especially on the legs, where one can apply a bandage. It is simpler than the method suggested by Dr. McFarland. It is true that when you first put the dressing on the itching and discomfort may be accentuated, but if you can get the patient to leave the dressing on for 24 hours he is usually relieved, and, as Dr. McFarland said, the dressing should be left on preferably for two or three weeks and not disturbed.

When much moisture or infection is present, the method is not practical. I have deliberately treated eruptions of this type with "Zinax" dressing but found that the dermatitis tends to get worse under the occlusive dressing.

DR. HERMAN V. ALLINGTON, Oakland, Calif.: I have several times seen patients with new areas of dermatitis adjacent to an occlusive dressing applied in treating chronic pruritic dermatoses. When unable to reach the involved area, they have instead rubbed and scratched the adjoining skin and reproduced the dermatitis at this new site.

DR. ALBERT R. McFARLAND, Rochester, N. Y.: It is probably true, as Dr. Rothman suggests, that a single trauma may at times be a precipitating cause of cancer. In fact, I had such a case just a few weeks ago. A 56-year-old man had struck his forehead on a cupboard door six weeks prior to my seeing him. Examination showed a well-developed basal cell epithelioma about 1 cm. in diameter. However, percentage-wise these cases are not impressive. Until we really know the cause of cancer, such incidents must be considered merely a link in the chain of events which results in cancer.

I think Dr. Ellis has already answered Dr. Rothman's question as to the itching after applying protective dressings in cases of lichen simplex. I always warn patients that there will be considerable itching for two or three days after applying the dressing. However, if they will stick it out for a few days, the itching will let up. Upon their return at the end of two weeks, they almost routinely say, "For the past 10 days, Doctor, I have had practically no itch." Of course, these occlusive dressings cannot be used if infection is present and cannot be employed unless the site of the lesion lends itself to bandaging.

I am glad to hear Dr. Ayres say that some of his patients with acarophobia have recovered. Perhaps I have not followed such patients long enough. I will say this, that most of these patients seem to be rather normal persons except for the delusion of things crawling on their skins. I must say that my attempts at therapy in these cases have been quite futile.

DISEASES RELATED TO LIGHT SENSITIVITY

BEATRICE MAHER KESTEN, M.D.
NEW YORK
AND
MEYER SLATKIN, M.D.
BROOKLYN

ALTHOUGH Willan in 1798, in describing eczema solare, suggested sensitivity to sunlight and Bazin in 1860 gave the name hydroa to a group of bullous lesions precipitated by sunlight, kindling of interest in light sensitivity has come within our time. The discovery of photosensitizers, particularly the porphyrins, in the early 1920's, placed undue stress on the association of light sensitivity with porphyrin excretion. Recent studies by Blum,[1] Brunsting,[2] Epstein [3] and Lamb [4] and their co-workers have dealt with various facets of the complicated problem of light sensitivity.

The present discussion revolves about the classification of cutaneous reactions to sunlight; the identification of the action spectra producing light sensitivity, and the use of chemical sunscreens.

The sun's rays concerned with light sensitivity range from approximately 2,900 to 8,000 A. In this spectrum ultraviolet lies between 2,900 and 3,900 A., visible light between 3,900 and 7,700 A., and infrared beyond 7,700 A. The action spectrum of the sunburn erythema lies between 2,900 and 3,170 A., with maximum effect at 2,967 A. It is within the ultraviolet that most sensitivity to light occurs.

From the Department of Dermatology, Columbia University, College of Physicians and Surgeons.

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I. CLASSIFICATION

Cutaneous reactions to sunlight have been classified previously, but, as Epstein [3] noted, gaps in our knowledge preclude a scientific arrangement. The schematic classification in Table 1 is an attempt to bring together, in a somewhat orderly and less complicated manner, eruptions following exposure to sunlight.

TABLE 1.—*Schematic Classification of Diseases Related to Light Sensitivity*

I. Occurring in Apparently Normal Skin

A. Solar erythema
- Erythema with or without edema
- Erythema multiforme type

B. Chronic polymorphic light dermatitis
- Eczema type
- Prurigo type

C. Solar urticaria produced by
- Ultraviolet
- Visible light
- Infrared light

D. Photodynamic dermatosis
- Photochemical
- Phytophotodermatosis
- Coal tar melanosis

II. Occurring in Skin that is Presumably Abnormal
- Porphyria and porphyrinuria
- Hydroa vacciniforme
- Epidermolysis bullosa
- Xeroderma pigmentosum
- Light sensitivity associated with infection
- Light sensitivity associated with endocrine disturbance

III. Occurring as Koebner Phenomenon
- Pellagra and pellagroid eruptions
- Lupus erythematosus
- Keratosis follicularis (Darier's disease)
- Pityriasis rubra pilaris
- Papular urticaria
- Rarely in: scleroderma, dermatomyositis, allergic eczema, lichen planus, and psoriasis

IV. Occurring in Skin After Prolonged Exposure to Sunlight
- Chronic sunburn with or without keratoses
- Degeneration of collagen and elastic tissue
- Epithelioma

GROUP I. LESIONS OCCURRING IN APPARENTLY NORMAL SKIN

In this group are placed the lesions of well patients with apparently normal skin until exposed to sunlight. Usually after minimal exposure one of the following reactions occurs.

A. Solar Erythema.—In this group of lesions belongs the transient erythema or erythema and edema that develops shortly after minimal exposure to sunlight. More persistent erythema and erythema-multiforme-like lesions (erythema solare perstans) have been observed by Lamb [4] and others. These abnormal reactions are probably due to the ultraviolet spectrum. The erythema, dryness, and itching of the

skin reported by Bresler [5] which followed prolonged exposure to fluorescent lights at short range and which was remedied by encasing the lights in plate glass, apparently belong to this group.

B. Chronic Polymorphic Light Eruptions.—This name, given by Haxthausen,[6] to both the eczematous and the prurigo-like eruptions in light-sensitive patients includes many morphologically similar eruptions.

In the eczematous type might be included the localized plaques of dermatitis occurring particularly in our Southwest [4] and the more widespread pruritic vesicular dermatitis to which have been given the names contact dermatitis type, eczema perstans solare, eczema solare, and light sensitization—adult group.

In the prurigo type might be placed the predominantly pruritic urticaria-like papular and nodular lesions. Summer prurigo, prurigo aestivalis, and prurigo simplex chronica recidivans fall in this group.

The majority of patients tested have been sensitive to ultraviolet light and usually within the sunburn spectrum.

C. Solar Urticaria.—Rather uncommonly, brief exposure of otherwise normal patients to sunlight is followed shortly by an outbreak of urticaria confined to the areas exposed. If exposure is prolonged, generalized urticaria, edema, and syncope may follow. About 40 cases have been reported.

In 26 adequately studied patients, 15 reacted only to ultraviolet rays. In four this was limited to the sunburn spectrum. Four reacted to both ultraviolet and visible light. In six urticaria was produced by the blue-violet of visible light. Watkins [7] reported one case of sunlight urticaria reproduced only by luminous heat in the near infrared region. Duke [8] observed localized and later generalized urticaria in a patient following physical burns, which he called urticaria ab igne. In cholingeric urticaria [9] localized or generalized urticaria may be produced routinely by exposure to infrared rays.

D. Photodynamic Dermatoses.—Tappenheimer [1] gave the name photodynamic action to the sensitization of a biologic system to light by a substance serving as a light absorber for photochemical reactions in which molecular oxygen takes part. This was in contrast to ultraviolet effects, which may take place either in the presence or in the absence of oxygen. Biophysical studies of wave lengths of light responsible for exciting photodynamic action show that only those wave lengths which are absorbed by a system can produce photochemical reactions in that system. Therefore a considerable degree of coincidence can be expected between the action spectrum of sunlight producing photodynamic action and the absorption spectrum of the sensitizing substance. While one cannot predict what will happen to a given molecule which absorbs a quantum of radiation, the possibilities are fluorescence,

5. Bresler, R. R.: Cutaneous Burns Due to Fluorescent Light, J. A. M. A. **140**:7, 1949.

6. Hausmann, W., and Haxthausen, H.: Die Lichterkrankungen der Haut: Strahlentherapie; Sonderbände, Berlin, Urban and Schwarzenberg, 1929, Vol. 11.

7. Watkins, A. L.: Infra-Red Urticaria, Arch. Phys. Therap. **24**:291, 1943.

8. Duke, W. W.: Urticaria Caused by Light, J. A. M. A. **80**:1835, 1923; Urticaria Caused Specifically by the Action of Physical Agents, ibid. **83**:3, 1924.

9. Hopkins, J. G.; Kesten, B. M., and Hazel, O. G.: Urticaria Provoked by Heat and Psychic Stimuli, Arch. Dermat. & Syph. **38**:679, 1938.

chemical reaction, increase in potential energy, and ionization. Fluorescence is a characteristic of the skin and of many of the substances causing photosensitization. It is thought that the photodynamic agent becomes fixed to the cells, and its action is comparable to that of a catalyzer. The accumulation of the sensitizing substance in the target area enhances the absorption of incident ultraviolet energy. This, in turn, increases the histamine-absorption rate and accounts for the biologic phenomena. Photodynamic substances may cause absorption in the ultraviolet spectrum and emit longer wave lengths in the visible light, which, in turn, act as sensitizers. Absorption may also occur in the visible light spectrum.

Under photodynamic dermatoses are grouped the various substances producing photosensitivity of the skin (Table 2).

TABLE 2.—*Substances Reported to Produce Photodynamic Dermatoses*

- Photochemical Dermatoses
  - Endogenous
    - Dyes
      - Eosin
      - Erythrosin
      - Fluorescein
      - Methylene blue
      - Rose bengal
      - Acriflavine
    - Porphyrins
    - Arsphenamine
    - Barbiturates
    - Quinine
    - Sulfonamides
    - Gold
    - Phenothiazine
    - Plants
      - Chemopodiaceae (goosefoot, pigweed)
      - Hypericaceae (St. John's-wort)
  - Exogenous
    - Dyes
      - Eosin
      - Erythosin
    - Coal tar
    - "Dyed fabrics"
    - Sulfonamides
    - *p*-Aminobenzoates
      - Monoglyceryl
      - Isobutyl
- Phytophotodermatoses
  - Ammieeae (cow parsnip, parsley, masterwort, angelica)
  - Cruciferae (mustard)
  - Gramineae (meadow grass)
  - Moraceae (fig)
  - Pastinaeae (parsnip)
  - Rosaceae (agrimony)
  - Ranunculaceae (buttercup)
  - Rutaceae (gas plant, rue, bergamot orange, Persian lime)
  - Berlock dermatitis
    - Cologne water
    - Perfume
    - Bergamot oil
    - Citron oil
  - Coal tar melanosis
    - Coal tar pitch, residue, and oil distillates
    - Lianthral

As shown in Epstein's [10] experiments with sulfanilamide, by Sams [11] with plants, and Kuske [12] with plant oils, the photodynamic reaction in the skin may be either phototoxic or photoallergic.

Photochemical Dermatoses: Of historic interest are the observations that dyes, porphyrins, and some barbiturates given parenterally sensitized the skin to sunlight. Acriflavine, a known photosensitizer, was used therapeutically to enhance the action of ultraviolet rays in dermatitides. More recently sulfonamides have been noted to sensitize the skin and have been used similarly. Sulfonamides, coal tar, dyes, and rarely derivatives of paraaminobenzoic acid may produce photosensitivity when applied to the skin. The photosensitizing effect of acriflavine, sulfonamides, barbiturates, and rose bengal is within the sunburn spectrum, while that of coal tar and porphyrins is in the visible light range.

10. Epstein, S.: Photoallergy and Primary Photosensitivity to Sulfanilamide, J. Invest. Dermat. **2**:43, 1939.

11. Sams, W. M.: Photodynamic Action of Lime Oil, Arch. Dermat. & Syph. **44**:571, 1941.

12. Kuske, H.: Cutaneous Plant Photosensitivity, Dermatologica **82**:273, 1940.

Phenothiazine, an insecticide, has produced photosensitivity in a few orchard workers, probably by inhalation of the fumes.

Animal Photosensitivity: Hypericism, a serious disease of domestic animals, particularly sheep, is due to photosensitivity following the eating of St.-John's-wort. Among the symptoms are marked itching and a severe dermatitis, particularly of the areas not covered by wool. It is much severer in light-colored animals. Effective measures, other than eradicating the plant, have been painting the animals, introducing dark-colored breeds, shearing in the late summer, and, when possible, protecting them from sunlight. The photosensitizing substance, hypericin, has an absorption spectrum in the visible light range.

Fagopyrism, producing a similar photosensitivity in animals, has not been as adequately studied. It may follow eating buckwheat, agave, lucerne, and vetch.

Phytophotodermatitis: Instances of photosensitization following sunbathing in meadows were reported before Oppenheim produced the name dermatitis striata pratensis bullosa for this effect. When traumatized moist skin has come into contact with plant juices and been subjected to sunlight, dermatitis of varying degree and pigmentation may follow. Kuske found that five plants (rue, parsnip, cow parsnip, fig, and angelica) producing this form of photosensitivity had a common sensitizer, furocoumarin, which absorbed wave lengths from 3,340 to 3,660 A. It is probable that photosensitivity to plants is produced by near ultraviolet and violet light.

The peculiar localized patches of pigmentation which Freund in 1916 traced to the action of sunlight on skin to which cologne water had been applied probably belong in this group. Now known as Berlock dermatitis, this type of photosensitization occurs after the application of certain toilet waters, perfumes, citron, and bergamot oil. Kuske, experimenting with a distillate of bergamot oil extracted from the photosensitizing plant masterwort, demonstrated its absorption spectrum to be from 2,800 to 4,100 A. However, Blum, after reviewing the literature on Berlock dermatitis, felt that bergamot oil sensitized the skin to blue and violet light.

Coal Tar Dermatitis and Melanosis: It has long been recognized that in workers handling coal tar pitch, its distillates, and residues a dermatitis followed by pigmentation develops when they work out of doors. Lianthral and carboneol, as well as other coal tar preparations which penetrate the corneum, may render the skin sensitive to light. Foerster and Schwartz,[13] in testing photosensitive workers with fresh coal tar pitch and five of its derivatives, found the action spectrum for these sensitizers to lie between 3,900 and 5,000 A. Chronic melanosis or shagreen has been reported by Ross[14] following close prolonged contact with coal tar, oils and pitch and exposure to sunlight. As protective creams that were opaque to ultraviolet rays proved helpful, sunlight seemed a contributing factor.

Group II. Diseases Occurring in Skin That Is Presumably Abnormal

This group comprises the dermatoses of light-sensitive patients with inherited abnormalities, disturbed porphyrin or endocrine metabolism, and certain infections. Because of the rather frequent association of abnormal quantities or types of urinary

13. Foerster, H. R., and Schwartz, L.: Industrial Dermatitis and Melanosis Due to Photosensitization, Arch. Dermat. & Syph. **39**:55, 1939.

14. Ross, P.: Occupational Skin Lesions Due to Pitch and Tar, Brit. M. J. **2**:369, 1948.

porphyrins with light sensitivity, a few remarks on porphyrins are included. A more comprehensive study is to be found in the writings of Watson [15] and Zeligman.[16]

Porphyria and Porphyrinuria.—Porphyrins in various complex arrangements, acting as respiratory pigments, form one of the most important systems found throughout plant and animal life. Normally less than 300 γ daily of coproporphyrin types I and III is eliminated in the urine. Excretion of urinary coproporphyrins in excess of this amount is termed porphyrinuria. It is often associated with disturbed liver function. The appearance of uroporphyrins in the urine, except in traces, is a requirement for the diagnosis of porphyria. The tendency to excrete abnormal kinds and amounts of porphyrin is inherent and often familial in persons with porphyria. Its activation, either early in life or in adulthood, may be linked with skin lesions which are adversely affected by sunlight. Since Hausmann's discovery of the photosensitizing action of porphyrins, many workers have endeavored to prove that porphyrins were or were not the photodynamic substances in light-sensitive patients. The problem remains unsolved, although experiments with most of the porphyrins on man and animals have resulted almost uniformly in marked photosensitization and the appearance of dermatitis, wheals, or hydroa-like lesions. These reactions occurred more frequently to the visible and infrared spectrum than to ultraviolet. The absorption spectra for porphyrins range from 3,000 to 6,500 A., with intense absorption bands, depending on the type of porphyrin, between 3,000 and 4,100 A. and between 5,060 and 6,020 A.

Congenital Porphyria and Hydroa Vacciniforme.—In congenital porphyria, in which light sensitivity is a common feature, uroporphyrin type I is found in the urine and feces as well as increased amounts of coproporphyrin. Porphobilinogen is absent. By fluorometric methods porphyrins have been observed in the skin of persons with congenital porphyria.[1] As noted by Zeligman, in about one-third of 200 cases of hydroa vacciniforme the disease was associated with congenital porphyria. The most famous patient in this group is that of "case Petry" which has been extensively recorded by Fischer.[1] In this patient lesions could be produced by sun or ultraviolet light. Urine from this patient, which showed an absorption spectrum in the region of 5,340 to 6,170 A., sensitized white mice to sunlight. In other rare instances hydroa-like lesions have been produced by exposure to sunlight or to ultraviolet between 3,250 and 3,960 A. Abnormal sensitivity to sunlight, to the spectrum between 3,200 and 4,500 A., has been observed in about 10 cases. However, about an equal number of observers have been unable to demonstrate any sensitivity to sunlight.

Ochronosis: The counterpart of congenital porphyria in animals is ochronosis, which may occur in cattle or swine. It is frequently associated with photosensitization. Lesions occur on regions not covered by hair and, more particularly, in white animals. Excessive amounts of both uroporphyrin and coproporphyrin are found in the urine.

Adult Acute Porphyria.—In adults suffering from acute intermittent porphyria eruptions are rare. Pigmentation or, exceptionally, erythema with vesiculation may

15. Watson, C. J., and others: Porphyria: Clinical Manifestations in Relation to Chemical Findings, Minneapolis, Minn., University of Minnesota Staff Meeting Bulletin *22*, No. 7, Nov. 7, 1950.

16. Zeligman, I.: The Relationship of Porphyrin Metabolism to the Dermatoses, Thesis, Columbia University, New York, 1942.

appear, but it has not been shown that these abnormalities are due to the action of sunlight. Uroporphyrin III and usually porphobilinogen together with an increased amount of coproporphyrin III are present in the urine.

Chronic Porphyria and Epidermolysis-Bullosa-Like Lesions.—As ably shown by Brunsting, it is the cutaneous lesions of chronic porphyria that may first suggest the diagnosis of disturbed porphyrin metabolism. The complexion takes on a dusky-red hue and epidermolysis-bullosa-like lesions follow exposure to sunlight, heat, or trauma. Milia, melanosis, and hypertrichosis may be present. About a dozen other reports note the association of epidermolysis-bullosa-like eruptions with porphyria. Efforts to reproduce the lesion by exposure to sunlight have been unsuccessful, although it is possible that sunlight may render the skin more sensitive to trauma. Uroporphyrins and porphobilinogen are found in the urine, and there may be an increased excretion of coproporphyrin in this disease. The presence of liver damage, often associated with alcoholism, suggests an interference with normal bile formation.

Geeldikopf: In this serious disease of sheep obstruction of biliary excretion is followed by jaundice. If the sheep are exposed to sunlight, marked photosensitivity with pronounced edema of the head and later necrosis of the skin, fever, and starvation may follow. As worked out by Quin,[1] a specific porphyrin which is a normal product of digestion in ruminants enters the blood stream of the affected animals and leads to increasing concentrations in the skin and to photosensitivity. Although Quin has rendered sheep photosensitive to this porphyrin, it has not been established that animals suffering from geeldikopf are sensitive to the same wave lengths of light as animals sensitized by injection of this porphyrin.

Porphyrinuria.—The increased excretion of coproporphyrin may occur in diverse pathologic conditions as well as dermatoses. Adequate studies by Brunsting, by Zeligman, by Gomez Orbaneja [17] and by others on porphyrinuria in a variety of skin diseases tend to show that more patients with photodermatoses have increased coproporphyrin than those with other dermatoses. Porphyrinuria has been reported in almost all diseases associated with light sensitivity, more particularly in lupus erythematosus and in alcoholic pellagra. The presence of abnormal amounts of coproporphyrin in the urine is not considered a diagnostic test for photosensitivity.

Hydroa Vacciniforme and Epidermolysis Bullosa.—In these two diseases with inherently abnormal skin, even when not accompanied by porphyria, aggravation or precipitation of lesions may be associated with exposure to sunlight. Although experimental attempts to elicit lesions have been unsuccessful, increased sensitivity to sunlight has been noted.

Xeroderma Pigmentosum.—Photophobia and the evolution of lesions in the patients with xeroderma pigmentosum suggest a photosensitivity in this disease. However, efforts to demonstrate the presence of a photodynamic substance in the blood or urine have been almost uniformly unsuccessful. Although characteristic lesions have not been reproduced experimentally, extensive investigations on a few patients have at times demonstrated an increased sensitivity of the skin to the sunburn spectrum. Persistent pigmentation in a few and erythema with telangiec-

17. Gomez-Orbaneja, J., and Castro-Mendoza, H. J.: Dermatosen und Porphyrie, Dermatologica **94**:327, 1947.

tases in one [18] followed the erythema produced by ultraviolet light. It may be that sunlight accelerates the disease process in this inherited abnormality.

Light Sensitivity Associated with Infections.—The presence of infections may induce or facilitate temporary or intermittent photosensitivity. Among the virus infections, herpes simplex appears rather commonly after exposure to sunlight. Photosensitivity has followed measles, intercurrent epidemic infections, lymphogranuloma inguinale, and vaccinia (in men taking sulfanilamide). Bacterial infections of the skin, respiratory tract, and gastrointestinal tract, especially of the gallbladder, may on occasion induce photosensitivity. As found by Stokes,[19] treatment of a localized bacterial infection of the skin with ultraviolet light may produce a widespread photodermatitis and a decreased tolerance to ultraviolet light on the part of the infected skin.

Light Sensitivity Associated with Endocrine Dysfunction.—The successful treatment of a variety of light-sensitive eruptions with steroid and gonadotropic hormones suggest that normal steroid metabolism may be interfered with by abnormal reactions to sunlight or that sensitivity to sunlight may occur in patients with abnormal steroid metabolism. Temporary photosensitivity, appearing as dermatitis, urticaria, or hydroa-like lesions, has been noted by a few observers in association with menstrual disturbances. Correction of this disturbance with estrogenic substances banished or greatly reduced the reaction. D'Amato,[1] however, observed a patient who was freed from photosensitivity only during the time menses were inhibited by radiotherapy. In three patients with solar urticaria and menstrual disturbances reported by Wucherpfennig,[1] wheals were produced only by the ultraviolet spectra.

Group III. Diseases Occurring as Koebner's Phenomenon?

The observation of Koebner that mechanical, physical, or chemical agents may bring out typical lesions during the irritative state of psoriasis suggests that a similar effect may be produced by sunlight in patients with other diseases. In this group are placed the diseases of patients with nutritional or hereditary diseases and skin lesions with a distinguishing dermatologic morphology in whom lesions characteristic of the disease have been produced by exposure to sunlight.

Pellagra and Pellagroid Eruptions.—As noted by Ormsby and others, in the acute stages of pellagra characteristic lesions may be produced by exposure to sunlight. It is not the ultraviolet spectrum which produces the reaction. Smith and Ruffin [20] produced lesions quite as effectively with an electric heater as with sunlight. Hypersensitivity to heat might explain the distribution of the lesions and their occurrence during the season of greatest insolation.

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18. Rothman, S.: Research on Xeroderma Pigmentosum, Arch. Dermat. u. Syph. **144**:440, 1923.

19. Stokes, J. H., and Callaway, J. L.: Pyogenic Relapse and Sensitiveness to Light in Certain Dermatoses, Arch. Dermat. & Syph. **36**:976, 1937. Stokes, J. H.; Beerman, H., and Ingraham, N. R.: Photodynamic Effects in Dermatology, Am. J. M. Sc. **203**:608; **204**:601, 1942.

20. Smith, D. T., and Ruffin, J. M.: Effect of Sunlight on the Clinical Manifestations of Pellagra, Arch. Int. Med. **59**:631, 1937.

Pellagroid eruptions have been noted in alcoholics, more particularly ones on deficient diets with liver damage. Starving persons who have eaten pigweed and shortly gone out in the sun have been found to acquire pellagra-like lesions going on to blisters and deep ulcerations. Grzybowski [21] was unable to reproduce the lesions in these patients by exposure to ultraviolet light.

The war melanosis of Riehl, reported in 1918, in which bronzed pigmentation appeared largely on the exposed skin of starving persons existing on bread made from beans, probably belongs to the group of pellagroid eruptions.

Lupus Erythematosus.—The history of severe sunburn preceding the outbreak of discoid or acute disseminated lupus erythematosus is not rare. Exceptionally dissemination of lesions follows the treatment of a localized patch with ultraviolet rays. Various authors have observed that in some patients exposure to sunlight aggravated or precipitated an attack. Zarafonetes [22] found five of eight patients hypersensitive to tests with ultraviolet light. He noted a favorable response to oral ingestion of sodium paraaminobenzoic acid, which is a sulfonamide antagonist and chemical sunscreen. Davidson,[23] after observing an immediate relapse in a patient with discoid lupus erythematosus following ultraviolet therapy, administered quinine in the hope that it might change the reaction of the skin to ultraviolet light. He and others observed remissions following oral administration of quinine and the application of protective ointments. Garzon [24] reproduced the lesion by exposure of a patient with subacute lupus erythematosus to ultraviolet light. In an area similarly exposed but protected by a sunscreen no lesion appeared. Garzon was of the opinion that antiactinic creams provide excellent protection against light factors, which figure prominently in this disease.

Keratosis Follicularis and Pityriasis Rubra Pilaris.—In these two hereditary gene dermatoses, particularly the former, new lesions or an aggravation of existing lesions has been noted in areas exposed to sunlight. Preissmann [25] induced typical lesions in apparently normal skin in two patients with keratosis follicularis (Darier's disease) by repeated exposures to ultraviolet light.

Other Skin Diseases.—Rarely typical attacks of allergic eczema, lichen planus, and psoriasis have been precipitated by exposure to sunlight or ultraviolet therapy. The seasonal incidence and location of lesions in children with papular urticaria suggest that exposure to sunlight may intensify the disease. O'Donnell [26] observed improvement in papular urticaria of adults when the areas were protected by clothing, and he expressed the view that light plays a part in the production of lesions in some cases of this disease. Earlier reports suggest sensitivity to sunlight in isolated instances of patients with scleroderma and dermatomyositis.

21. Grzybowski, M.: Peculiar Pellagra-like Skin Sensitization to Light in Starving Persons, Brit. J. Dermat. **60**:410, 1948.

22. Zarafonetes, C. J. D.; Greken, R. H., and Curtis, A. C.: Further Studies on the Treatment of Lupus Erythematosus with Sodium Paraaminobenzoate, J. Invest. Dermat. **11**:359, 1948.

23. Davidson, A. M.: Quinine Bisulfate as a Desensitizing Agent in the Treatment of Lupus Erythematosus, Arch. Dermat. & Syph. **37**:247, 1938.

24. Garzon, R.; Ferraris, L., and Cancio, C.: Experimental Study of Lupus Erythematosus, Rev. argent. dermatosif. **33**:106, 1949.

25. Preissmann, M.: Provocative Action of Light in Darier's Disease, Ann. dermat. et syph. **6**:188, 1946.

26. O'Donnell, J. M.: Observations on Lichen Urticatus and Light, M. J. Australia **1**:766, 1948.

GROUP III. DISEASES OCCURRING IN SKIN AFTER PROLONGED EXPOSURE TO SUNLIGHT

Although proof is lacking, it is assumed that sunburn radiation enters into the pronounced persistent changes occurring on uncovered areas of skin after excessive or prolonged living out-of-doors. Among the changes noted are persistent freckles, degeneration of collagen and elastic tissue, and chronic sunburn with or without warty excrescences.

Several experimenters have induced dermatoses on the ears of rats and mice by repeatedly exposing them to excessive doses of ultraviolet light. Sunburn, telangiectases, keratoses, warts, and often infiltrating carcinomas developed.

Recent statistical reports tend to support the view that prolonged excessive exposure of fair-skinned blue-eyed persons to sunlight may, in certain ones, stimulate the production of malignant tumors.

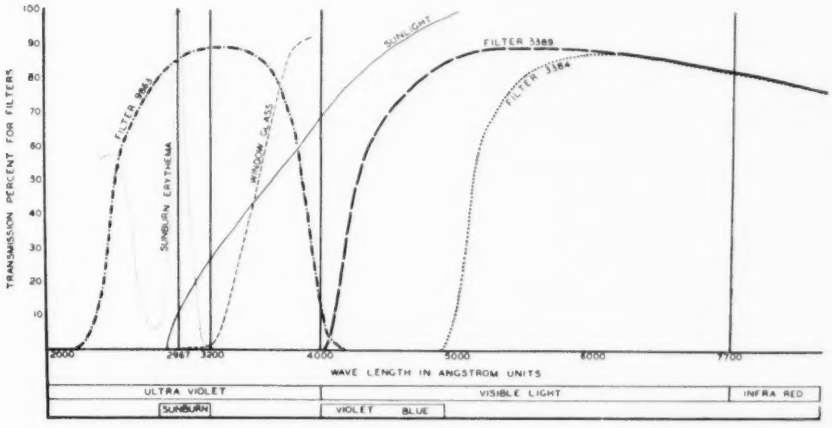

Chart 1.—Approximate light transmittance of Corning glass color filters. Filter 9863 transmits ultraviolet light. Ordinary window glass transmits ultraviolet light beyond the sunburn spectrum. Filter 3389 transmits visible light. Filter 3384 transmits visible light beyond the blue-violet spectrum.

II. IDENTIFICATION OF THE ACTION SPECTRA PRODUCING LIGHT SENSITIVITY

In reviewing the literature on diseases associated with light sensitivity, proof that absorption of sunlight is the activating mechanism is often lacking. As seen in the preceding section, a number of patients were hypersensitive to sunlight and to part of its spectrum. In very few instances has a lesion characteristic of the individual patient's disease been induced by sunlight or by specific wave lengths within sunlight. This would seem a necessary requirement for proof of light sensitivity. Blum, in particular, has emphasized the importance of identifying the wave lengths effective in eliciting abnormal biological responses. In diseases produced by light the first step must be the absorption of a quantum of radiation by some substance in the skin. Since all substances absorb radiation of certain lengths, a clue to the nature of the light-absorbing substance might be given by the wave length which produces the lesions. He suggested classifying light-sensitive diseases into skin lesions produced only by radiation which induces sunburn of normal skin and skin

lesions due to abnormal photosensitizing substances in the skin elicited by wave lengths beyond the sunburn spectrum. Ordinary window glass may be used for the experimental separation of the two. This classification appears to be incomplete.

Colored filters and more recently monochromatic light and Corning glass color filters [27] (spectral transmitting filters) have been used to help define the wave lengths producing light sensitivity. By means of one of these methods most of the

TABLE 3.—*Summary of Data from Cases of Suspected Light Sensitivity*

Case	Diagnosis	Sex	Age, Yr.	History of Dermatitis	Sunlight Action Spectrum, A	Comment
Solar Erythema						
1	Erythema and edema	F	42	Exposed areas, 3 yr.	< 3,200	Protected by 15% *p*-aminobenzoate cream
2	Erythema and edema	M	48	Exposed areas, 25 yr.	< 3,500	Protected by "A°-fil" or "skolex" cream
3	Erythema-multiforme type	M	33	Diffuse, 6 yr.	< 3,900	Relief with 15% *p*-aminobenzoate cream and tripelennamine by mouth
Chronic Polymorphic Light Eruption						
4	Eczema type	F	56	Exposed areas, 10 yr.	< 3,400	Protected by "A°-fil" cream
5	Eczema type, urticaria	M	28	Exposed areas, 8 yr.	< 3,400	Protected by 10% "sunarome" ointment
Solar Urticaria						
6	To ultraviolet	F	35	Exposed areas, 6 yr.	< 3,700	Protected by "A°-fil" cream
7 *	To visible light (blue-violet)	F	46	Generalized, since childhood	4,000-5,000	Slight relief with tripelennamine by mouth
8 *	Xeroderma pigmentosum	M	3	Diffuse, 2 yr.	< 2,800	No hypersensitivity; erythema and pigmentation produced
9 *	Keratosis follicularis	F	46	Worse in summer, 30 yr.	< 3,900	Erythema on minimal exposure
10 *	Keratosis follicularis	M	37	Lesions followed radiotherapy	< 3,200	Lesions on minimal exposure; reproduced with Kromayer light
Lupus Erythematosus						
11	Discoid type	F	46	Lesions precipitated by sun, 20 yr.	< 3,900	Erythema on minimal exposure; atypical lesion produced by repeated exposure to Kromayer light
12	Subacute type	F	36	Worse on exposure to sun, 1 yr.	< 3,900	Erythema on minimal exposure; atypical lesion produced by repeated exposure to Kromayer light

* These patients were presented from Vanderbilt Clinic at meetings of the New York Academy of Medicine.

experimental lesions induced in light-sensitive patients have followed absorption of ultraviolet light. A few were sharply limited to the sunburn spectrum, and others, such as the photodynamic and pellagroid eruptions, were independent of it. With use of monochromatic light and filters, most detailed studies on patients with solar urticaria have shown that wheals can be induced within several specific wave lengths of sunlight.

27. Glass color filters were obtained from Corning Glass Works, Optical Sales Department, Corning, N. Y.

In our experience, window glass and Corning filters have been of value in determining the approximate action spectra in sunlight which induces sensitivity. The light-transmittance curves of some of them is shown in Chart 1. The transmittance of Corning filter 9863 is in the ultraviolet spectrum, and lesions induced only by the action of sunlight through this filter preclude sensitivity to visible or infrared light. Ordinary greenish window glass transmits light beyond 3,200 A. and is useful in eliminating reactions to the sunburn spectrum. Corning filter 3389 transmits visible and infrared light and is useful in eliminating reactions to ultraviolet light. Corning filter 3384 transmits light beyond the blue-violet of visible light. It, together with filter 9863, detects sensitivity to blue-violet light.

Case Studies of Light Sensitivity.—Attempts were made to determine the action spectra producing the lesions in 12 patients who gave a history of hypersensitivity to light. As shown in Table 3, the first seven had apparently normal skin, and in the first six there was hypersensitivity to ultraviolet light. (By hypersensitivity is meant that the amount of sun or Kromayer light required to produce just perceptible erythema, noted as M. E. D., was appreciably smaller than that required to produce an erythema in normal patients of comparable age and skin color.) Complete or partial protection was afforded by chemical sun screens in the first six patients. Following the suggestion of Rubin and co-workers,[28] oral administration of tripelennamine afforded some increase in tolerance to sunlight in two patients (Cases 3 and 7). In patients with solar erythema (Cases 1 and 2) and with urticaria (Cases 6 and 7), lesions characteristic of the respective diseases could be reproduced by exposure only to the wave lengths noted. In the patients with solar urticaria, wheals could not be produced by injection of acetylcholine or the application of ethyl chloride or hot water.

Of the last five patients, all of whom had abnormal skin, all except the one with xeroderma pigmentosum (Case 8) were hypersensitive to ultraviolet light. In one patient with keratosis follicularis (Case 10) a typical lesion, both histologically and clinically, was produced on his normal-appearing skin by one exposure to 8 M. E. D. (eight seconds) of Kromayer light. In the other (Case 9) repeated similar exposures produced only sunburn. In both patients with lupus erythematosus (Cases 11 and 12) lesions typical of the disease clinically were produced by repeated applications of 3 to 4 M. E. D. of Kromayer light. Histological comparison of a lesion produced experimentally in each patient with the patient's spontaneous lesions showed the former to be somewhat atypical. The skin of the child with xeroderma pigmentosum (Case 8) was not sensitive to sunlight, although photophobia was prevented only by wearing polaroid glasses. Numerous tests with a number of Corning filters with sun or Kromayer lamp as the source of light showed that erythema and pigmentation were produced on the uninvolved skin only by wave lengths less than that found in solar radiation. After a year's treatment with 15% paraaminobenzoic acid ointment locally and paraaminobenzoic acid and tripelennamine orally, there has been only a slight increase in freckling of the skin.

28. Rubin, L.; Beal, P., and Rothman, S.: A Method for Protection of Patients with Solar Urticaria, J. Invest. Dermat. **8**:189, 1947.

Application of ethyl chloride, of adhesive tape to an area for 10 days, or of heat, by means either of fomentations or of infrared rays, failed to produce any lesions on the apparently normal skin of these patients.

The tests on these patients suggest that sensitivity to light is to that portion within the ultraviolet spectrum. Amelioration of symptoms might be expected from the application of substances which absorb ultraviolet light.

III. SUNBURN PROTECTION

Sun Screens

Experience tells us that accommodation to sunlight in the normal skin is achieved by gradual exposure to the actinic rays of the sun. Thickening of the horny layer of the skin subsequent to exposure to sunlight is the main mechanism by which accommodation occurs. Not only does the horny layer absorb light strongly in the ultraviolet part of the spectrum, but the flattened and granular layers reflect and scatter light, thus effectively preventing it from reaching the sensitive prickle cells below. Measurements of transmission of sunburn radiation by the skin show that a considerable degree of protection would be afforded by relatively slight thickening of the horny layer. In addition to this thickening, sweating and tanning offer some protection against sunburn. Human sweat, owing to its absorption of wave lengths of less than 3,300 A., provides some protection against sunburn. As the sunburn injury to the skin is largely in the prickle-cell layer, melanin pigment laid down in the basal layer after exposure to sunlight offers little protection. It is only as the pigment granules later migrate outward in small quantity that the melanin serves to protect the prickle cells.

Under optimal conditions for sunburn, only 0.2% of the total solar radiation is erythemogenic, and this fraction is found between wave lengths 2,900 and 3,200 A. According to Luckiesh,[29] 90 to 95% of this erythemal radiation is absorbed by the normal white skin. In correlating the wave lengths of solar radiation with their erythemal effectiveness in the untanned skin, he found that at 2,925 A. there was an erythemal effectiveness of 70% ; at 2,967 A. it rose to 100% ; at 3,024 A. it had dropped to 50%, and at 3,132 A. there had been a steep decrease to 2%. It appears, then, that artificial protection from sunburn should be afforded by a screen which scatters or absorbs most of these rays which produce the sunburn erythema.

The problem of sunburn protection is a complex one, and for a more detailed study reference to the work of deNavarre[30] and particularly to that of Giese[31] is suggested.

Commercial sunburn preventives usually consist of a chemical which absorbs the sunburn spectrum incorporated in a suitable vehicle. In addition, some contain a chemical which because of its physical properties scatters light. Of these titanium dioxide is perhaps the most suitable and widely used. Others are talc, kaolin, zinc oxide, calamine, magnesium oxide or stearate, calcium carbonate, and lithopone.

29. Luckiesh, M.: Application of Germicidal, Erythemal and Infra Red Energy, New York, D. Van Nostrand Company, Inc., 1946.

30. deNavarre, M. G.: The Chemistry and Manufacture of Cosmetics, New York, D. Van Nostrand Company, Inc., 1941.

31. Giese, A. C., and Wells, J. M.: Sunburn Protection, Natural and Artificial, Scient. Month. **62**:458, 1946. Christensen, E., and Giese, A. C.: Photosensitivity of Sun Screens, J. Am. Pharm. A. (Scient. Ed.) **35**:223, 1950.

The vehicles themselves may have a limited capacity to absorb erythemal radiation. As noted by Giese,[32] carbolated petrolatum (carbolated vaseline®) and petrolatum have considerable value, while white liquid petrolatum and lanolin have almost none. Several of the vegetable oils have limited absorptive power, sesame oil being the most effective as shown by Orelup.[33] After a detailed study of some 100 formulations of newer vehicles, Giese [34] found the most satisfactory to be a vanishing cream of methylcellulose in water in which was incorporated 20% homomenthyl salicylate and 10% titanium dioxide, bentonite, magnesium, and butyl stearates, with pigments added to produce the desired color.

The so-called "sun screens," i. e., chemicals, which absorb light in the ultraviolet but not in the visible part of the spectrum, which now number over 100, represent a comparatively recent development. The first in the United States appeared in 1928. Previous to this time, fluorescent natural products, such as quinine, esculin, and tannic acid, were used. Most of the recent sun screens, according to Giese, are aromatic compounds, and the benzene rings and double bonds usually present are the chromophores which absorb the erythema-producing rays of sunlight. A detailed list has been presented by de Navarre and also by Giese. The latter has classified a number of these compounds into families and studied the absorption spectra of some 25 of the members. The main families of compounds are paraaminobenzoates, orthoaminobenzoates, salicylates, cinnamates, pyrrones, benzimidazoles, carbazoles, naphthol sulfonates and quinine compounds. Giese found the following, in the dilutions tested, to be excellent sun screens: menthyl and homomenthyl salicylate and ethyl and isobutyl paraaminobenzoate. The salicylates as a whole appeared to be good sun screens and most of the others tested were satisfactory. Some of the pyrrones, naphthol sulfonates, and menthyl anthranilate absorbed rays as long as 4,000 A. Klarman [33] found the absorption spectra of paraaminobenzoic acid to be far superior to that of the ortho or meta isomers. Kumler and Daniels [35] found monoalkyl and dialkyl paraaminobenzoate esters to have five to eight times the screening power of salicylates, three times that of the umbelliferones, and twice that of the unsubstituted paraaminobenzoate compounds. The dark red veterinary petroleum developed by Luckiesh [36] affords excellent protection from sunshine but has limited use in civilian life.

Hazelton [37] lists the following as points of value in choosing a sun screen for normal skin. The sun screen should absorb rays below 3,200 A., with the maximum efficiency of absorption at 2,967 A., and transmit most rays beyond 3,200 A. This protection should be obtained with the thinnest possible film, as the application to the skin is probably between 0.02 and 0.08 mm. in thickness. It should not be toxic, irritating, or allergenic, even when applied to large areas over a protracted time.

32. Giese, A. C.; Christensen, E., and Jeppson, J.: Absorption Spectra of Some Sun Screens for Sunburn Preparations, J. Am. Pharm. A. (Scient. Ed.) **39**:30, 1950.

33. Orelup, J. W., cited by Klarman, E. G.: Sunburn and Suntan, The American Perfumer, July and August, 1949.

34. Giese, A. C., and Wells, J. M.: Sweat- and Water-Resistant Sunburn Preparations, J. Am. Pharm. A. (Scient. Ed.) **35**:208, 1946.

35. Kumler, W. D., and Daniels, T. C.: Sunscreen Compounds, J. Am. Pharm. A. (Scient. Ed.) **37**:474, 1948.

36. Luckiesh, M.; Taylor, A. H.; Cole, H. N., and Sollman, T.: Protective Skin Coatings for Prevention of Sunburn, J. A. M. A. **130**:1, 1946.

37. Hazelton, L. W.; Groopman, J., and Morrish, E. P.: Physical, Pharmacological, and Dermatological Studies on a Sunscreen, Proc. Sc. Sect., Toilet Goods A., No. 13, May 1950.

The compound should be stable, so that its properties do not change with varying pH of the skin, nor should it deteriorate on exposure to air or absorbed rays. It should not discolor the skin or clothing or rub off easily. Although in most instances one should be able to remove the sun screen with soap and water, perspiration or a short swim should not render it ineffectual. The sun screen should maintain its effectiveness for at least several hours. From the practical point of view, it should be cosmetically acceptable and the cost should be reasonable.

Most of the properties of a sun screen and the vehicle in which it is incorporated are subject to laboratory study, but the value of a sunburn preventive lies in the prevention of injury by the sunburn spectrum to the normal or to the abnormal skin.

To this end, the effectiveness of the preparation as shown by Giese may be ascertained by first determining the minimal dose of sunshine required to cause

TABLE 4.—*Commercial Sunburn Preventives*

Key	Name of Preparation	Sunscreening Agent		Absorption Spectrum (A.) (90% absorption between)
1	"Solar cream"	*p*-Aminobenzoic acid Titanium dioxide	4% 15%	.....
2	"Dorothy Gray sunburn cream"	Isobutyl *p*-aminobenzoate Dipropyleneglycol salicylate	...	2,400-3,400
3	"Tartan"	Monoglyceryl *p*-aminobenzoate	...	2,800-3,050
4	"Gypsy suntan lotion"	Monoglyceryl *p*-aminobenzoate	2.5%	2,600-3,200
5	"Skolex cream"	Propylene glycol *p*-aminobenzoate	4%	2,500-3,200
6	"Dara sun tan lotion"	Isobutyl *p*-aminobenzoate 2-ethylhexanediol-1, 3	2% 30%	.....
7	Norwich® greaseless sun tan lotion	Glyceryl aminobenzoate Ethyl aminobenzoate	2.9% 0.5%	2,900-3,200
8	"A°-fil cream"	Menthyl *o*-aminobenzoate Titanium dioxide	5% 5%	2,900-3,750
9	"Gypsy suntan oil"	Benzyl salicylate Benzyl cinnamate	2% 2%	2,480-3,280
10	"Helena Rubinstein sun and wind proof cream"	Glyceryl salicylate	...	.....
11	Sutra®	Hydroquinone	5%	2,700-3,100
12	"Sunprotectol"	Digalloyl trioleate	5%	2,900-3,150
13	"A°-fil sun stik" (lip stick)	Digalloyl trioleate	2.5%	2,880-3,400
14	"Helena Rubinstein liquid sunshine"	2-Ethylhexanediol-1, 3	20%	.....
15	"Ardena sun pruf cream #2"	2-Ethylhexanediol-1, 3	20%	2,900-3,400

a just perceptible reddening of the skin (M. E. D.). Once the M. E. D. has been determined, measured areas of skin may be thinly coated with the sunburn preventive and exposed to sunlight and the exposure time required for 1 M. E. D. through the preventive noted. Blum [1] has calculated that even under the most extreme conditions no more than 20 M. E. D. units of erythemic radiations fall on a person on a given day. Giese [32] has suggested that "sunburn preventives" be graded as to their protective value in minimal erythema doses (M. E. D.) with and without the vehicle and that the ingredients used should be listed. To the extent that a given product is represented as a preventive for sunburn, the label is required to state the ingredients to which the prophylactic effect is attributed.

No product should protect so completely as to prevent some erythemic response after long exposure if it is to prevent the sunburn in the normal person, since only with exposure is natural adaptation acquired. In the abnormal skin it may be necessary to filter out longer wave lengths as well as the sunburn spectrum.

Commercial Sunburn Preventives

Table 4 lists sunburn preventives together with pertinent data, much of it obtained through the cooperation of the manufacturers. This includes only preparations that are labeled as preventing sunburn or blocking out most of the rays producing sunburn. Antihistaminic creams, some of which have high extinction peaks in zones producing sunburn, are not included because of the facility with which they sensitize the skin. Although a number of chemical families are represented, all the preventives listed, with the possible exception of "tartan," are excellent absorbers of the maximum erythemogenic effect of the sun, which occurs at 2,970 A.

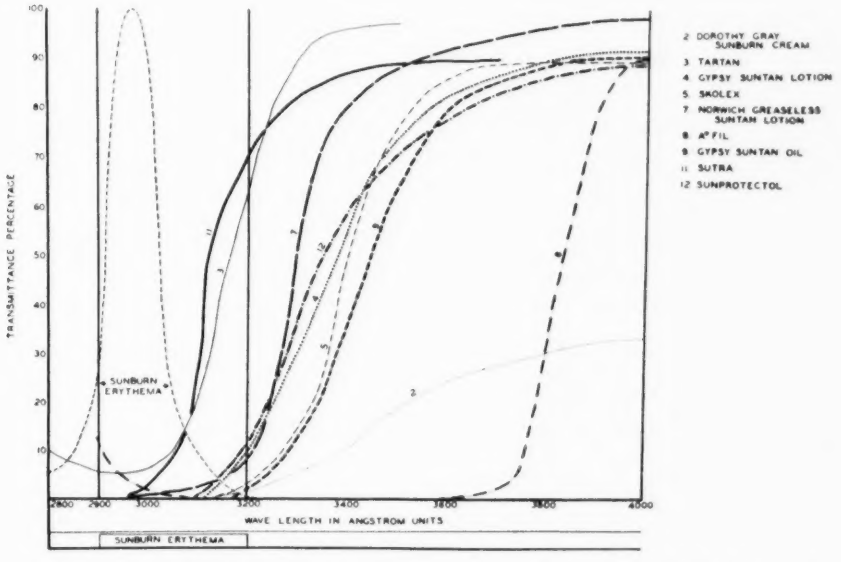

Chart 2.—Approximate sunlight transmittance curves of nine commercial sunburn preventives. Almost all offer complete protection from the "sunburn erythema." (Wave lengths between 2,900 and 3,170 A.)

Commercial Sun Screens.—Chart 2 contains the approximate sunlight transmittance curve of nine commercial preparations. With the exception of "tartan" and "sutra," protection from the entire sunburn erythema (2,900 to 3,200 A.) is excellent. Dorothy Gray sunburn cream and "A°-fil" afford considerable protection beyond the sunburn erythema.

Preliminary Studies with Sun Screens.—A study of the clinical efficacy of sun screens has been organized as follows. The time required to produce a just perceptible erythema (M. E. D.) following exposure to Kromayer light was ascertained on 50 patients. Fifteen 1-in. (2.54 cm.) square areas were blocked off with adhesive tape. To each of 14 of these areas was applied thinly one of the commercial sunburn preventives listed in Table 4 (Nos. 7 and 13 were not tested). Carbolated petrolatum was similarly applied to the 15th square. Each area then received 10 M. E. D. of Kromayer light. The M. E. D. for each patient had been determined previously.

"Solar cream" afforded complete protection in almost all patients. To a lesser degree and in the order given the following protected most patients from 10 M. E. D.: Carbolated petrolatum, "skolex," "Helena Rubenstein sun and windproof cream" and "Dorothy Gray sunburn cream." The remainder of the sunburn preventives provided little protection to most of the patients tested by this method.

Similar experiments with eight chemical sun screens incorporated in hydrophilic ointment were performed on 30 patients.

Ointments incorporating 15% paraaminobenzoic acid[38] and the one containing 5% cycloform® (isobutyl paraaminobenzoate) offered excellent protection. Each of the following ointments afforded little protection, 5% menthyl orthoaminobenzoate; 5% of 2 parts menthyl orthoaminobenzoate and 5 parts ethylene glycol monosalicylate; 5% "heliophan" (homomenthyl salicylate); 10% "sunarome" O (2 ethylhexyl salicylate), 5% "filtrosol A," and 5% "filtrosol B" (salicylate family).

Preliminary studies under these conditions suggest that only a few sun screens and carbolated petrolatum protect the skin from half the erythemic radiation (10 M. E. D.) that might fall on a person on any given day. Studies in progress suggest that a number protect the skin from 4 to 5 M. E. D. of Kromayer light.

SUMMARY

A classification of diseases related to light sensitivity is suggested.

The use of light-transmitting filters for the delineation of wave lengths in the solar spectrum producing sensitivity to sunlight is discussed. By this means hypersensitivity to varying spectra in sunlight has been demonstrated in 11 patients. In five patients lesions typical of the patient's disease, and in another two patients atypical lesions, were produced by exposure to Kromayer light.

Data on a number of chemical sun screens which absorb a part of this spectrum are presented.

ABSTRACT OF DISCUSSION

DR. JOHN LAMB, Oklahoma City: I wish to congratulate Dr. Kesten on an excellent presentation of a very involved and interesting subject—allergic manifestations of light and their effect on the skin. The classification presented is both adequate and comprehensive.

Any attempt to classify the polymorphic light-sensitive eruptions is disconcerting, since many plaque-like eruptions start as an erythema solare and by excoriation and chronicity become thickened and plaque-like, mixed with pruriginous lesions.

The use of hormones in treating these eruptions has been successful only in those persons who have had the persistence to continue this therapy for 12 to 18 months.

Chronic hepatitis from infections, as in syphilis or amebiasis, and in alcoholics is another factor in the treatment of these patients. Since the estrogens cannot be properly inactivated by a diseased liver, there is consequently a high level of circulating estrogens. This, in turn, causes an inhibitory effect upon the trophic hormones of the pituitary, which produces atrophy of the testes.

Thus, the low levels of testosterone in the skin may cause incomplete enzymal reactions in the tyrosine to the melanin system which may account for the depigmented, pinkish color of many of the lesions. Therefore, because of the lack of the screening ability of black melanin, the dermal vessels and collagen are subjected to the effects of strong sunlight. High dosage of vitamin B complex and vitamin C is another necessary adjunct in the treatment of this group.

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38. Rothman, S., and Rubin, J.: Sunburn and PABA, J. Invest. Derm. **6**:445, 1942. Rothman, S., and Henningsen, A. B.: The Sunburn Protecting Effect of PABA, ibid. **9**:307, 1947.

Dr. Kesten's series of patients with various light dermatoses were carefully studied to determine the action spectra of wave lengths inducing the light sensitivity in each disease, but the ability to reproduce the lesions in each disease was disappointing, as it was in our series. In our plaque-like types we could not reproduce the lesions with a single exposure to the various action spectra, but we felt that the plaques were produced by repeated solar injuries from many exposures.

Sunfilter creams have played a part in the protection of many of our patients. The colored creams have been satisfactory to men, but most women prefer the nonoily alcohol preparations.

The antihistamines have not been tried by our group because we have given full support and study to hormonal methods. However, many of our patients have had these chemicals before coming to us, without effect.

Again I want to congratulate Dr. Kesten on an excellent paper.

DR. STEPHEN ROTHMAN, Chicago: I should like to comment on two points. One is that the absorption coefficient of paraaminobenzoic acid in the sunburn range is 500 times greater than that of orthoaminobenzoic (or anthranilic) acid. Still it has been claimed that anthranilic acid is as good a sun screen as the para- compound. I was glad to hear that Dr. Kesten's observation confirms biologically what has been evident from physical measurements, namely, that paraaminobenzoic acid is far superior to anthranilic acid in its sun-screening potency.

My second comment concerns the use of esters of paraaminobenzoic acid. Commercial firms exploiting our findings on paraaminobenzoic acid have concocted sun-screening preparations using esters instead of the free acid because it is easier to make smooth creams with the esters. Unfortunately, however, the esters are much more potent sensitizers than the free acid. The latter is a polar compound; its absorption into the epidermis is limited, and therefore it hardly ever causes sensitization. In this way, most unfortunately, a good preparation has been brought into miscredit. I still maintain that 15% paraaminobenzoic acid in a vanishing cream base is the best sun-screening preparation there is (Rothman, S., and Rubin, J.: Sunburn and Para-Aminobenzoic Acid, *J. Invest. Dermat.* **5**:445, 1942; Rothman, S., and Henningsen, A. B.: Sunburn-Protecting Effect of Para-Aminobenzoic Acid, ibid. **9**:307, 1947). It protects against the most intense solar radiation that ever occurs on earth, and its sensitizing potency is minimal. If by the use of esters sensitization is produced the use of the free acid will also be prevented.

DR. LOUIS A. BRUNSTING, Rochester, Minn.: I have enjoyed very much this excellent presentation by Dr. Kesten. The various factors which may contribute to light sensitivity have been enumerated. In many respects the mechanism of action in photosensitive dermatoses is still a mystery. In his book on "Photodynamic Action and Diseases Caused by Light,"[1] Harold F. Blum outlines the postulates that must be fulfilled in order to prove the relationship between symptoms and a particular sensitizing agent. So far as I know, these postulates have been fulfilled only in the case of Southdown sensitivity in sheep, by Clare, of New Zealand, who found that newborn lambs of porphyria heritage became photosensitive only when chlorophyll substances were added to the diet. The particular sensitizing agent in the blood was found to be a porphyrin product of chlorophyll, phyloerythrin. In hypericism and phagopyrism, sensitivity to porphyrins is suspected but not proved.

In some of the diseases in man that are associated with sensitivity to light, namely porphyria, pellagra, and lupus erythematosus, there is evidence of a disordered hepatic function. This may offer a valuable clue to the elucidation of the mystery of photosensitivity in humans.

DR. BEATRICE M. KESTEN: We are now recognizing the value of Dr. Rothman's pioneer work which showed that paraaminobenzoic acid is an excellent sun screen.

BIRTHMARKS IN INFANTS

A. G. PRATT, M.D.
CAMDEN, N. J.

AN INTEREST in hemangiomas led to the examination of 1,096 infants to determine the natural rate of occurrence of the so-called strawberry mark. I had been unable to find this information in recent textbooks of dermatology and in other available literature. At the same time a record was kept of all other birthmarks.

All the infants were examined in the maternity nurseries of the Cooper Hospital, Camden, N. J. It was recognized that many strawberry marks are not present at birth but appear shortly thereafter. Accordingly, the examinations were made as near the end of the infants' stay in the hospital as possible. The great majority were between 4 and 8 days old. Of the 1,096 infants, 879 were white and 217 were Negro or part Negro. They were nearly evenly divided between boys and girls.

STRAWBERRY MARK

The strawberry mark was detected in 10 of the 879 white infants and 3 of the 217 Negro infants, or slightly over 1% of each race. All the lesions were solitary, except in one white infant who had four. Those on the white infants were bright ruby red in color, while those on the Negro infants were darker bluish red. A few lesions were small red puncta, though the majority ranged from 0.5 to 2 cm. in diameter. All but the smallest were distinctly elevated.

There was no anatomical preference. The 16 lesions were located on 13 different areas. There was one each on an upper eyelid, cheek, forearm, shoulder, posterior axillary fold, thoracic portion of the back, lumbar portion of the back, abdomen, hip, scrotum, and thigh. There were three about the knee and two on the leg.

It is common knowledge that the strawberry mark may not make its appearance at birth or immediately thereafter. Two cases illustrate this fact. One white infant had no visible lesion when examined at the age of 7 days. He was kept in the nursery because of prematurity, and when reexamined at the age of 20 days had a prominent red hemangioma. The attending nurse reported that the mark was first noticed at the age of 11 days. Another white infant was examined when 7 days old and had no hemangiomas except a naevus flammeus nuchae and a similar violaceous discoloration of the left upper eyelid. Three months later, the infant was brought to the hospital for treatment of a typical strawberry mark approximately 0.6 cm. in diameter on the right side of the abdomen.

From these cases, it is obvious that the figure of 1% represents the rate of occurrence during the first week of life, and that the true total rate must be somewhat higher.

Associate Professor of Dermatology, Jefferson Medical College of Philadelphia.

NAEVUS FLAMMEUS

The term naevus flammeus brings to mind the purplish macular vascular birthmark which covers a considerable part of a side of the face and persists throughout life, and for which there is no satisfactory treatment. Only one such example was found among the 879 white infants and none among the Negroes. The one example was on the right side of the face of a girl. There were, however, three other instances of port-wine stain among the white infants—a bluish-red macule 3 cm. in diameter on a buttock, and two similar macules involving eyelids.

Naevus Flammeus Nuchae.—This term refers to the minor form of port-wine stain common to adults and infants at the back of the neck. It is a pinkish or violaceous capillary hemangioma without elevation or palpability. Extreme irregularity of outline is the rule, and the margins are distinct. It may consist of one intricately shaped lesion or multiple smaller ones. The most quoted rate of occurrence in infants is that of Pollitzer (40 out of 114)[1] and De Paul,[2] who stated that 30 out of each 100 infants are born with this lesion at the back of the neck. Corson [3] reported finding this mark at the nape in only 6 of 210 newborn infants, although such appearances were numerous elsewhere, notably on the eyelids.

I found this lesion in 370 of the 879 white infants (42%) and 66 of the 210 Negro infants (31%). Without excellent lighting it is difficult to detect the lesion in the Negro infants, especially if there is a good growth of hair.

Nuchal Type Found Elsewhere.—I prefer to separate this group from the typical port-wine stain for clinical reasons. The minor type of naevus flammeus found chiefly on the face is a close counterpart of the naevus flammeus nuchae in that it is extremely irregular in outline and only slightly violaceous, although it may seem quite prominent to the anxious parents. They can be assured, however, that the mark will spontaneously disappear, usually within the first three to six months of life. It occurred as follows:

	White Infants	Negro Infants
Right upper eyelid	95 (11%)	25 (12%)
Left upper eyelid	98 (11%)	17 (8%)
Forehead	41 (5%)	13 (6%)
Nose	9 (1%)	7 (3%)
Upper lip	5	5
Back	5	..
Right buttock	2	..
Cheek	1	1
Chin	1	1
Scrotum	1	..
Scalp	1	..
Axilla	1	..

Some of the infants had the nuchal type at the back of the neck alone and a few had it elsewhere alone, though usually if there was a lesion on the face it also

1. Pollitzer, S., in Bangs, L. B., and Hardaway, W. A.: An American Textbook of Genito-Urinary Diseases, Syphilis and Diseases of the Skin, Philadelphia, W. B. Saunders Company, 1898, p. 1006.

2. De Paul, cited by Crocker, H. R.: Diseases of the Skin: Their Description, Pathology, Diagnosis, and Treatment, with Special Reference to the Skin Eruptions of Children and an Analysis of 15,000 Cases of Skin Disease, Ed. 3, Philadelphia, P. Blakiston's Son & Company, 1907, p. 962.

3. Corson, E. F.: Nevus Flammeus Nuchæ: Its Occurrence and Abnormalities, Am. J. M. Sc. **187**:121-124 (Jan.) 1934.

occurred at the nape. The total number of infants with this type of birthmark on at least one area was 421 white (48%) and 84 Negro infants (39%).

OTHER VASCULAR BIRTHMARKS

One cavernous angioma involving the entire left middle finger of a Negro infant was seen. No other vascular birthmarks were observed except those enumerated previously.

PIGMENTED NEVI

The diagnosis of pigmented nevus was made for the white infants when a distinctly tannish, well-marginated macule from 0.5 to 1 cm. in diameter was seen. There was one such lesion present in only 24 of the 879 white infants (2.7%). If one agrees that nearly all adults have one or more pigmented nevi, then it is apparent that the great majority of pigmented nevi of white persons are not present at birth but appear at some time after the first few days of life.

In the Negro infants the macular type of pigmented nevus was found more frequently, and some nevi were multiple. There was one lesion each in 29 infants, two lesions each in 4 infants, and three lesions in 1 infant. The total of 34 infants gave an average of 15.6%.

No elevated pigmented nevi, hairy pigmented nevi, or blue nevi were found.

MONGOLIAN SPOT

The type of pigmentation known as Mongolian spot was present in 5 of the 879 white infants, or a little more than 0.5 of 1%. One girl had a well-marginated, slate-colored area of pigmentation about 4 cm. in diameter at the upper part of each buttock. A boy had a similar mark about 3 cm. in diameter over the sacrum. A second boy had a Mongolian spot about 6 cm. in diameter over the upper part of the right buttock and a smaller one over the sacrum. A third boy had a very irregular slate-gray discoloration extending across the sacral area to each buttock. The remaining example consisted of four macules, one at the crest of the ilium, and three clustered about the sacrum, each from 1 to 2 cm. in diameter.

Niedelman,[4] in describing pigmented lesions of the Negro, stated that he had never found a Mongolian spot on a white infant. Epstein[5] described seeing 25 Mongolian spots in 20 years of practice among German children under circumstances in which he thought there was no possibility of Negro admixture. He estimated the frequency of Mongolian spots in white children at about 1 in 600.

The Mongolian spot was common among the Negro infants, occurring in 131 of 217. The marks were usually quite noticeable, often covering the entire buttocks and sacral region, and some infants had multiple lesions, with Mongolian spots on the wrists, shoulders, knees, and ankles, as well as the usual sites. As Brennemann[6] said, they never occurred on flexor surfaces. It was the rule that if a spot occurred

4. Niedelman, M. L.: Abnormalities of Pigmentation in the Negro, Arch. Dermat. & Syph. **51**:1-9 (Jan.) 1945.

5. Epstein, A.: Über den blauen Kreuzfleck und andere mongoloide Erscheinungen bei europäischen Kindern, Jahrb. Kinderh. **62**:60-73 (Jan.) 1906.

6. Brennemann, J.: The Sacral or So-Called Mongolian Pigment Spots of Earliest Infancy and Childhood, with Especial Reference to Their Occurrence in the American Negro, Arch. Pediat. **24**:426-444 (June) 1907.

on one of the less common areas, there would be one at the buttocks or sacral region. There was only one exception.

In Negro infants, the Mongolian spot was often accompanied by other types of birthmark. Twelve also had a pigmented nevus; 37 also had the minor form of naevus flammeus which I have termed the nuchal type; 14 also had both a pigmented nevus and a nuchal type of hemangioma, and one had both a Mongolian spot and a strawberry mark.

Niedelman examined 103 newborn Negro infants and found 41 with Mongolian spots in the sacral area and only 5 with spots elsewhere. Brennemann, on the other hand, examined 40 Negro children under one year of age, half being less than one week old, and found 35 had well-marked Mongolian spots.

MISCELLANEOUS BIRTHMARKS

There were two instances of supernumerary ears among the 879 white infants, and two Negro infants had extra digits. One of the white infants had a fibroma of the scalp, and a Negro infant had a fibroma at the rim of the ear.

The rate of occurrence of birthmarks has not been given separately for the two sexes, because there was little variation between them.

SUMMARY

The presence of various types of birthmarks was determined in 1,096 infants (879 white and 217 Negro), the great majority being 4 to 8 days old. Strawberry marks occurred in 1.1% of the white and 1.4% of the Negro infants; the major type of naevus flammeus in 0.5% of the white and none of the Negro infants; the minor type of naevus flammeus in 48% of the white and 39% of the Negro infants; macular pigmented nevi in 2.7% of the white infants and 15.6% of the Negro; Mongolian spot in 0.5% of the white and 60% of the Negro infants. There were a few other less common birthmarks.

516 Cooper St.

Drs. Albert B. Davis and George B. German, attending obstetricians, Cooper Hospital, helped make this study possible.

EXPERIMENTAL STUDIES ON SARCOIDOSIS

Persistence and Survival of Inoculated Micro-organisms

A. ROSTENBERG Jr., M.D.
FREDERICK J. SZYMANSKI, M.D.
GEORGE J. BREBIS, M.D.
JOHN B. HAEBERLIN Jr., M.D.
AND
FRANCIS E. SENEAR, M.D.
CHICAGO

SARCOIDOSIS is a disease for which various etiologic and immunologic concepts have been advanced. Many have thought the condition to be of tuberculous origin. However, there were certain difficulties in the acceptance of the view of a tuberculous causation. The chief of these were that the tubercle bacillus could but rarely be cultured from patients with the disease and that the majority of persons with sarcoidosis manifested markedly reduced reactivity toward tuberculin. J. Jadassohn, in an endeavor to reconcile these findings with a tuberculous origin, hypothesized that persons with sarcoidosis actually had a special form of immunity toward the tubercle bacillus. He theorized that persons with this form of immunity disposed of the tubercle bacillus or its products so rapidly that the organism was rarely found or that the tuberculin did not have an adequate opportunity to produce its usual type of reaction. This theory has recently been considered in some detail by Rostenberg.[1]

To validate such a hypothesis, evidence would be needed to show that persons with sarcoidosis have an enhanced ability to dispose of the tubercle bacillus. We believed that the inoculation of living tubercle bacilli into patients with sarcoidosis and into control patients with a subsequent determination of (*a*) the persistence of the organisms in situ and (*b*) their viability would provide an appropriate test.

MATERIAL AND METHOD OF STUDY

For obvious reasons we were not in a position to use virulent tubercle bacilli; consequently we used the BCG strain of tubercle bacilli. We deemed it advisable to have a control organism to contrast with the BCG. For this purpose we were again constrained to select not only nonpathogenic organisms but also ones which would be readily identifiable and distinguishable from the resident skin flora. Mycobacterium smegmatis and/or Bacillus subtilis were chosen.[2]

From the Department of Dermatology (Dr. Rostenberg, Dr. Szymanski, Dr. Haeberlin, and Dr. Senear), the Allergy Unit (Dr. Rostenberg), and the Department of Medicine, University of Illinois College of Medicine.

1. Rostenberg, A., Jr.: Etiologic and Immunologic Concepts Regarding Sarcoidosis, A. M. A. Arch. Dermat. & Syph. **64**:385, 1951.

2. Dr. E. E. Vicher, of the Department of Bacteriology, University of Illinois College of Medicine, helped with the identification of the organisms.

The BCG organisms were introduced by the Rosenthal multiple puncture technique. This employs a steel plate about 1 by ¾ in. (2.5 by 1.9 cm.) with 36 projecting prongs which are approximately 1/16 in. 0.16 cm. in height. The material to be introduced is smeared over an area of the skin corresponding in size to the plate. The skin is then made taut by grasping and the projections forcibly pushed, by means of a metal device, through the inoculum. The contents of one capillary tube (0.1 ml.) were used.[3] The tubercle bacilli were inoculated into one arm and the selected control organism was inoculated into the other arm with the same technique. A 24-hour broth culture of the control organism was used, and approximately 0.1 ml. was spread over the skin surface.

Prior to the inoculations, the skin was cleansed with acetone. Alcohol and other antiseptics were deliberately not employed, so as not to reduce the viability of the introduced organisms. This meant that inevitably some of the surface flora were simultaneously introduced, but in no case did this seem to make any particular difference. Before the inoculations were done, the patients were tuberculin tested in order to determine at what dilution of old tuberculin (OT) they would fail to react. For a few control patients who were positive to a dilution of 1 : 5,000 or higher, the BCG vaccine was mixed with approximately equal parts of saline at the time it was introduced so that too severe a local reaction would be avoided.

Approximately at the fifth day, twelfth day, and around the sixth week biopsy specimens were taken, usually with a 5 mm. punch, from the BCG-inoculated site and from the control-inoculated site. Each specimen was bisected. One half was sent for pathological examination. The other half was minced for culture.

For pathologic examination all sections were stained with hematoxylin and eosin. The tissue from the BCG site was also stained with Ziehl-Neelsen stain and that from the control organism site with Gram stain. The sections were examined for (*a*) general histological appearance and (*b*) presence of bacilli.

For bacteriological examination the tissue was minced and small bits of it spread over the surface of Saenz's medium. Three tubes were inoculated with material from each specimen. The tubes were placed in an incubator held at body temperature and kept for three months. If at the end of this time there was no evidence of bacteriological growth, they were discarded and the culture labeled as sterile. If during this period growth appeared, it was examined for gross colonial characteristics. Smears were then made and stained for identification. If the organisms recovered from a BCG site resembled tubercle bacilli, to make certain of their nature tuberculin-negative guinea pigs were inoculated with the growth. Approximately three weeks after the inoculation the pigs were again tested with tuberculin. Only if they were now tuberculin-positive was the growth obtained from the specimens labeled as BCG.

Most of the subjects were quantitatively tested with old tuberculin in order to determine the end-points for positivity and negativity; i. e., a concentration was determined to which they would react, if necessary giving undiluted old tuberculin, and a dilution was also found to which they would fail to react. The majority of those so tested were retested after the BCG inoculation in order to determine what influence this had on the level of cutaneous sensitivity.

Thirteen patients with sarcoidosis and 11 patients with diseases other than sarcoidosis were used for the investigation. The evidence for the diagnosis of sarcoidosis is set forth in Table 1. It should be noticed that in all of the patients multiple systemic lesions were manifested.[4] Pertinent diagnostic information regarding the control cases is given in Table 2.

3. Dr. S. R. Rosenthal furnished generous supplies of BCG. The vaccine as distributed contains approximately 15 mg. of tubercle bacilli by dry weight per milliliter.

4. We believe it is extremely important to distinguish between the systematized disease sarcoidosis and a localized sarcoid reaction pattern. The latter denotes merely a certain type of pathologic picture which can be caused by a variety of causes, one of which is the tubercle bacillus. Another is the agent that causes sarcoidosis. In our opinion, much of the confusion in the literature and the explanation for the majority of the reports which are labeled as "sarcoid" or "sarcoidosis with positive bacillary findings" is due to a failure to make this distinction. It is probable the cases reported as instances of sarcoid with positive bacillary findings were for the most part cases of a sarcoid form of tuberculosis in which tubercle bacilli were found. In this paper whenever the term "sarcoidosis" is mentioned it is the systematized form of the disease which is considered.

RESULTS

We have assayed our results with respect to three points: (1) a comparison of the pathologic changes induced in the patients with and without sarcoidosis by the introduction of BCG and of control organisms; (2) the persistence in situ and the recoverability of the injected organisms in both groups of cases, and (3) the alteration, if any, in the degree of cutaneous tuberculin sensitivity by virtue of the experimental procedures.

TABLE 1.—*Clinical, Pathological, and Laboratory Findings in Cases of Sarcoidosis*

Case	Age, Yr.	Race	Sex	Skin Lesions	Lung Infiltrates	Lymph Adenopathy	Bone Lesions	Uveal Tract Involvement	Pre-BCG Tuberculin Sensitivity		Biopsy of ‡
									Positive *	Negative †	
1	29	N	F	0	Hilar	Hilar	0	+	1:5,000	1:20,000	Lymph node
2	11	W	M	+	0	Cervical	0	+	1:10	1:100	Lymph node
3	41	N	F	+	+	+	0	+	Undiluted	1:10	Skin
4	54	W	F	0	+	+ Splenohepatomegaly	+	+	1:100	1:1,000	Lymph node
5	28	N	F	+	+	0	0	0	1:100	1:1,000	Skin
6	46	N	F	+	+	0	0	0	1:100	1:1,000	Skin
7	33	N	F	+	+	+ Splenohepatomegaly	0	0	Undiluted	.....	Skin
8	49	N	F	+	+	+ Splenohepatomegaly	0	+	Undiluted	.....	Skin
9	51	N	F	0	+	+	0	0	1:100	1:1,000	Lymph node
10	40	N	F	+	+	+	+	0	Undiluted	.....	Skin
11	51	N	M	0	+	+	+	0	1:50,000	1:100,000	Thyroid
12	53	N	F	0	+	+	0	+	1:50,000	1:100,000	Lymph node
13	15	N	F	0	0	Hilar	0	+	Undiluted	1:10	.....

* Weakest dilution which elicited positive reaction.
† Strongest dilution which elicited negative reaction.
‡ Tissue showing sarcoid changes.

TABLE 2.—*Clinical Data Regarding Nonsarcoidosis Cases*

Case	Race	Sex	Age, Yr.	Diagnosis	Pre-BCG Cutaneous Tuberculin Sensitivity	
					Weakest *	Strongest †
1	W	F	36	Erythema induratum	1:1,000,000	.....
2	N	F	48	Chronic malaria	1:50,000	1:100,000
3	W	F	31	Lupus erythematosus	.....	.....
4	W	F	36	Pemphigus vulgaris	.....	.....
5	W	F	70	Acquired hemolytic anemia	1:5,000	.....
6	W	F	67	Pemphigus vulgaris	.....	.....
7	W	F	33	Pemphigus vulgaris; erythema multiforme	.....	.....
8	W	F	30	Chronic retinitis	1:1,000	1:5,000
9	W	M	67	Cirrhosis of liver	1:1,000	1:5,000
10	W	F	42	Duodenal ulcer	1:1,000	1:5,000
11	N	M	67	Pulmonary condition undiagnosed	1:20,000	1:50,000

* Weakest dilution eliciting a positive reaction.
† Strongest dilution eliciting a negative reaction.

Table 3 gives in a condensed fashion the pathologic changes resulting from the inoculation procedures. Before Table 3 is discussed, it might be pointed out that for the purpose of evaluating the data the pathologic changes were given one of three labels; normal, banal, or tuberculoid. By normal is meant that the changes

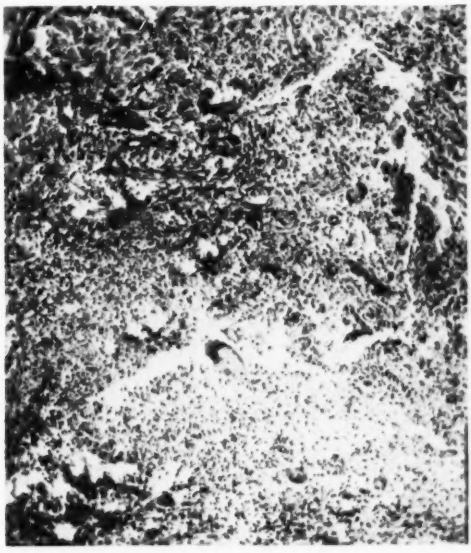


Fig. 1.—Section from a 10-day old lesion developing at the site of BCG inoculation in a patient with sarcoidosis.

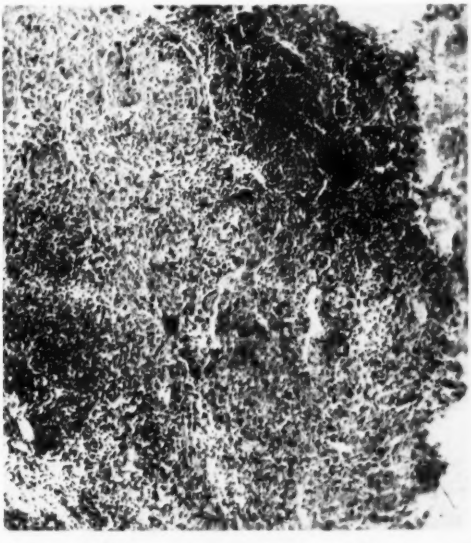


Fig. 2.—Section from a 43-day old lesion developing at the site of BCG inoculation in a patient with a disease other than sarcoidosis.

observed were so slight that for all intents and purposes the skin could be regarded as normal. By banal is meant that signs of inflammation were present. The inflammatory process was characterized by polymorphonuclear and round cells which tended to be clustered around the vessels of the upper cutis and were also massed in the corium at the site of the injection. By tuberculoid is meant that the changes seen had more specific characteristics. Epithelioid cells and Langhans' giant cells surrounded by lymphocytes with occasional mild necrosis were noted.

Parenthetically, it might be stated that in no case was the characteristic architecture of sarcoidosis found. From Table 3, it is evident that there is no essential difference between the ways the patients with sarcoidosis and the patients without sarcoidosis responded to the introduced organisms. In both groups there was a difference between the way the patients reacted to the BCG and to the control organism, but this difference was not determined by whether or not the patient had

TABLE 3.—*Types of Pathologic Changes Seen as a Consequence of BCG Inoculation*

	Subjects from Whom a Biopsy Specimen Was Taken, No.		Specimens Taken, No.		Specimens Showing Normal Response, %		Specimens Showing Banal Inflammation, %		Specimens Showing Tuberculoid Inflammation, %	
Diagnosis	BCG	Control *	BCG	Control *	BCG	Control *	BCG	Control *	BCG	Control *
Sarcoidosis.....	13	12	39	32	18	50	44	44	38	6
Not sarcoidosis....	11	7	34	19	9	37	50	58	41	5

* Control either M. smegma or B. subtilis.

TABLE 4.—*Visualization of Organisms in Sections and Growth on Culture Media* *

	Organisms Seen in Sections						Organisms Grown on Culture						Organisms Found Either in Sections or on Culture					
	Tubercle Bacilli			Control Organisms			Tubercle Bacilli			Control Organisms			Tubercle Bacilli			Control Organisms		
Diagnosis	T	?	+	T	?	+	T	?	+	T	?	+	T	?	+	T	?	+
Sarcoidosis.....	13	2	6	12	1	2	13	0	9	12	1	10	13	0	11	12	2	10
Not sarcoidosis	11	0	2	5	0	2	11	1	9	7	1	6	11	0	10	7	0	7

* T indicates the total number of subjects from whom the tissues were taken; ?, the number of subjects on whom there was an apparent success but in which there was some doubt as to the final identification, and +, the number of patients on whom the attempted procedure was successful.

sarcoidosis. The pathology of the lesions labeled as tuberculoid is illustrated in Figures 1 and 2. Figure 1 is a section from a 10-day old lesion at the site of the BCG inoculation in a patient with sarcoidosis; Figure 2 is a section from a 43-day old lesion at the site of the BCG inoculation in a patient with a nonsarcoid condition. It is evident that there is no difference in the pathologic changes observed in the two sections. It is also clear that the pathologic alterations depicted are not those of sarcoidosis.

Table 4 indicates how often organisms were either seen in the sections or grown in the cultures. It is clear that there is no significant difference between sarcoidosis and the other diseases with respect to the ability of the organisms either to persist in situ or to remain viable so as to be recoverable on culture.

Table 5 compares the cutaneous tuberculin sensitivity before and after the BCG inoculations. It will be noticed that here, too, there is no essential difference between the group with sarcoidosis and the group with other diseases.

COMMENT

Lemming [5] was apparently the first to endeavor to utilize the response to the introduction of living BCG organisms into patients with sarcoidosis as a diagnostic and interpretative tool. Since Lemming, various authors (Selander [6]; Weissenbach [7]; Saenz [8]; Sohier and Gregoire [9]; Leider, Sulzberger, and Hyman [10]; Cornbleet,[11] and Israel, Sones, Stein, and Aronson [12]) have employed this technique. All these studies were primarily concerned with the nature of the pathologic changes developing at the site of the inoculation and any alteration in the cutaneous tuberculin sensitivity brought about as a consequence of the inoculation. Leider, Sulzberger, and Hyman believed that the response induced by the BCG inoculation was different in the patient with sarcoid from that in the patient without sarcoid. Israel and associates, however, disagree with this opinion. They state, "Atypical local reactions occur at the site of vaccine in a small number of patients with sarcoidosis, but in the majority the local reaction is indistinguishable from normal."

In our experience, the time of first appearance, the rate of development, and the external morphology of the lesion developing at the inoculation site certainly could not be correlated with the presence or absence of sarcoidosis but was more correlatable, although imperfectly so, with the degree of tuberculin sensitivity. In

TABLE 5.—*Effect of BCG Inoculations on Level of Cutaneous Tuberculin Sensitivity* *

	Questionable Increase	No Change	Decrease	
			Questionable	Definite
Sarcoidosis	5	4	2	1
Not sarcoidosis	1	3	2	..

* By a questionable increase or decrease is meant that there was a 10-fold change in the end-point of reactivity; by a definite decrease, more than a 10-fold change in the end-point.

general, the gross lesion seen in the patient with sarcoidosis was just as intense and in no way distinguishable from the lesions which developed in the patients with diseases other than sarcoid. As can be seen from Table 3, the impression obtained

5. Lemming, R.: An Attempt to Analyze the Tuberculin Anergy in Schaumann's Disease (Boeck's "Sarcoid") and Uveoparotid Fever by Means of BCG Vaccination, Acta med. scandinav. **103**:400, 1940.

6. Selander, cited by Lemming.[5]

7. Weissenbach, R. J.: Maladie de Besnier-Bœck-Schaumann: Vaccination par le B. C. G.: Étude des réactions à la tuberculine, avant et après vaccination, Bull. Soc. franç. dermat. et syph. **48**:40, 1941.

8. Saenz, cited by Weissenbach.[5]

9. Sohier, R., and Gregoire, J.: Remarques sur le comportement après vaccination par le BCG-SP de deux sujets atteints de maladie de Besnier-Boeck-Schaumann, Bull. et mém. Soc. méd. hôp. Paris **61**:315, 1945.

10. (*a*) Leider, M., and Sulzberger, M. B.: Studies in the Allergy of Infection: Responses of the Skin to BCG Vaccination in Various Categories of Tuberculin Sensitivity, J. Invest. Dermat. **13**:249, 1949. (*b*) Leider, M., and Hyman, A. B.: Studies in the Allergy of Infection: Histologic Responses of the Skin to BCG Vaccination in Various Categories of Tuberculin Sensitivity, ibid. **14**:459, 1950.

11. Cornbleet, T.: BCG Vaccination in Sarcoidosis: Preliminary Report, Arch. Dermat. & Syph. **62**:697, 1950.

12. Israel, H. L.; Sones, M.; Stein, S. C., and Aronson, J. D.: BCG Vaccination in Sarcoidosis, Am. Rev. Tuberc. **62**:408, 1950.

from inspection of the gross lesions was borne out by the pathologic examination, inasmuch as there was no difference between the types of pathologic alterations noted in the patients with sarcoidosis and in the patients with diseases other than sarcoidosis. In order to determine whether or not a tuberculoid response was induced at a different rate in the patients with sarcoidosis, the average time in days at which this type of change was first noted in the section was calculated and compared with the time taken in patients with other diseases. For the patients with sarcoidosis this time was 37.6 days, whereas for the patients with other conditions it was 43.4 days. It would not seem that this difference is significant.[13]

The differences in the types of response engendered by the BCG and the control organisms are interesting and instructive to compare. It will be noticed that BCG evokes roughly the same percentage of tuberculoid type responses in patients with sarcoidosis as in other persons. The control organisms, while affecting the two groups equally so far as a tuberculoid response is concerned, called forth this type of reaction much less frequently than did the BCG. This would indicate that either (1) patients with sarcoidosis and patients with other diseases display the same immunologic reactions toward the tubercle bacillus or its derivatives or (2) a tuberculoid response in a person with sarcoidosis is determined not by the immune processes but rather by the nature of the antigen introduced. The first hypothesis is self-evidently not true, as shown by the disparity of behavior in the two groups toward tuberculin; consequently, we are forced to come to the second conclusion. Incidentally, this result illustrates the fallacy of the so-called Jadassohn-Lewandowsky law.[14]

No previous investigator compared the persistence or viability of tubercle bacilli in patients with sarcoidosis and in patients with other diseases. To us, from the point of view of the theory of positive anergy, this is the important consideration. For if there is any validity to the theory of positive anergy, which in essence asserts that the reason the person fails to react is because he actually disposes of the organism or products derived from it in an accelerated fashion, which, in turn, implies a form of immunity toward the organism, one should then be able to demonstrate a more rapid disappearance of the organisms from the site of introduction. One should also be less able to recover them on culture after a sojourn in the partially immune host. As can be seen from Table 4, such was not the case. There was absolutely no difference in the ability to recover the BCG organisms on culture

13. It should be realized that the actual average time noted is probably somewhat meaningless, since the tuberculoid response may have made its appearance considerably earlier than the time at which the biopsy specimen was taken; e. g., if the first specimen in which a tuberculoid response was noted was taken at the 60th day, then 60 days was the time used in calculating the average, but a specimen might not have been taken between the 12th day (at which time no tuberculoid response was noted) and the 60th day. These remarks of course apply equally to the cases in the two groups, and so, while the actual time is unknown, the information concerning the relative rates of development is probably valid.

14. Lemming.[5] The Jadassohn-Lewandowsky law, in essence, asserts that where bacteria are being slowly destroyed by antibodies tubercles and tuberculoid structures develop. Rich (Rich, A. R.: The Pathogenesis of Tuberculosis, Ed. 2, Springfield, Ill., Charles C Thomas, Publisher, 1951, p. 361), in considering the relation of hypersensitivity to tubercle formation points out that there is no acceptable evidence for believing the two are interrelated. He also believes that tubercle formation is related to the nature of the antigen rather than to the immune state of the host.

from patients with and from those without sarcoidosis. If anything, the tubercle bacilli were less well visualized in the sections from the patients without sarcoidosis, an observation which could be interpreted as indicating that the host who did not have sarcoidosis was putting up a better fight against the organisms than was the patient with sarcoidosis.

With regard to the alteration of the tuberculin sensitivity by the BCG inoculation, Table 5 indicates that we did not find any difference between the group with and the group without sarcoidosis. Leider and Sulzberger [10a] also did not observe any change in the cutaneous tuberculin sensitivity of their patients who did not have sarcoidosis as a consequence of BCG inoculation, but they did not comment on the possible significance of this.

We believe that this is an important finding, as those who favor the tuberculous causation of sarcoidosis and the theory of positive anergy have stressed that one of the main differences between patients with sarcoidosis and other persons lies in the different response to the inoculation of BCG. The group with sarcoid by and large do not attain cutaneous hypersensitivity, whereas a high percentage of the group without sarcoid attain it, the implication of this being that the failure to attain sensitivity is indicative of a resistance toward the tubercle bacillus. We should like to examine this comparison in some detail, inasmuch as we think that in most instances the comparison has been a faulty one. Let us consider for a moment the control group. This has nearly always been a group for which by virtue of age or because of negative roentgenologic and other clinical findings it could be stated that its members had not previously met the tubercle bacillus. As would be expected, when the initial infection with the organism develops (as a consequence of the BCG inoculation) immunological alterations evidenced by a positive cutaneous reaction develop.

Turning now to the patients with sarcoidosis: If the disease is on a tuberculous basis, then obviously the group has been infected with the tubercle bacillus and has had opportunity to develop immunological alterations toward it, but such patients, for reasons that need not detain us here, do not display an exalted skin sensitivity.[1]

The impropriety of the comparison is that one is comparing the influence of the BCG vaccination on a group that has met the tubercle bacillus with that of a group that has not, and the former group has a disease (sarcoidosis) and the latter has not. Thus, on the one hand, we have "sarcoidosis" and "exposure"; whereas, on the other, we have "no sarcoidosis" and "no exposure." In the comparison, the one variable (exposure) is ignored and the differences ascribed solely to the influence of the other variable (sarcoidosis). This is obviously unscientific and illogical, and, while conclusions drawn from such a comparison may be correct, they are not necessarily so. To put the argument in other words, the conversion from negative to positive skin reactivity in the control group after inoculation with BCG is to be expected, as this is presumably the subjects' first exposure to the tubercle bacillus, whereas the conversion in the cases of sarcoidosis is not to be expected, as the subjects already have encountered the tubercle bacillus and either failed to develop or lost a preexisting cutaneous reactivity. Now the point we wish to stress is that this may mean no more than that any group (regardless of diagnosis) which has already met the tubercle bacillus will not have its current level of cutaneous reactivity altered by additional exposure to the organism. Evidence for this view is furnished by the fact that a group of subjects without sarcoidosis did not have

the level of their skin reactivity shifted by additional new exposure to the tubercle bacillus. We feel that this possible explanation is an important one to understand, as it cuts away one of the props for the alleged immunity of patients with sarcoidosis to the tubercle bacillus. The known facts are more in accord with this thesis than any other so far advanced.

If it is not assumed that sarcoidosis is on a tuberculous basis and one had a group of cases for which there was no reason to believe a prior exposure to the tubercle bacillus existed, the aforesaid comparison would be a valid one, but what conclusions could then be drawn? Surely not that an immunity toward the tubercle bacillus exists but merely that for as yet unknown reasons a cutaneous sensitivity toward tuberculin develops with difficulty in patients with sarcoidosis.[1]

Actually the discussion of the preceding paragraph is to some degree academic, for on statistical grounds and in many cases on clinical grounds there is reason to believe that patients with sarcoidosis have met the tubercle bacillus. Consequently, regardless of the etiology of sarcoidosis, the first criticism as a rule applies to a comparison of the effect of BCG vaccination on patients with sarcoidosis with its effect on previously definitely nonexposed persons.

Now in our investigations the comparison was made between a group with sarcoidosis and another group of patients, a group without sarcoidosis but for which there was reason to believe they had previously been infected with the tubercle bacillus; consequently, there was only one variable, namely, the disease sarcoidosis. No difference so far as the effect of BCG vaccination on the cutaneous sensitivity was revealed.

Our work affords no evidence to support (1) the theory of positive anergy or (2) a tuberculous origin for sarcoidosis. We interpret the results of our investigations as arguing against both of these hypotheses.

SUMMARY AND CONCLUSIONS

Inoculations were made with living BCG organisms and living Mycobacterium smegmatis or Bacillus subtilis into 13 patients with sarcoidosis and 11 patients with diseases other than sarcoidosis.

No differences were noted between the patients with and those without sarcoidosis with regard to (1) the gross or pathologic alterations induced by the inoculations of the organisms, (2) recovery of the inoculated organisms, and (3) the change of cutaneous tuberculin sensitivity as a consequence of the BCG inoculation.

It is concluded that the theory of positive anergy is erroneous in that it implies that the failure to react is due to some exalted ability to dispose of the antigen or products derived from it. We do not assert that the failure of patients with sarcoidosis to react to tuberculin is on the same basis as that of the person who was never exposed. We do assert that the failure of people with sarcoidosis to convert from tuberculin negativity to positivity when inoculated with BCG is not due to the fact that they have any immunity toward the tubercle bacillus but is due to other, as yet unknown, reasons.

It is concluded that the tuberculous etiology of sarcoidosis is very unlikely.

News and Comment

NOTICES

Pacific Dermatologic Association.—The Pacific Dermatologic Association will hold its 1953 meeting at the Olympic Hotel and University of Washington in Seattle, on July 9 and 10, 1953. Dr. Earl Osborne will be the principal guest speaker and will lead symposia on "Cutaneous Malignancy" and "Industrial Dermatoses." Other features will include luncheon roundtable discussion groups, a clinical meeting, and a histopathologic seminar. Dr. Norman N. Epstein, of San Francisco, will preside as President. The 1954 meeting will be held at the Hotel Broadmoor, Colorado Springs, Colo. Nonmember dermatologists are welcome to attend the meeting.

Books

History of the American Dermatological Association in Commemoration of Its Seventy-Fifth Anniversary, 1876-1951. Paul E. Bechet, Editor. Price, $10. Pp. 392, with 294 illustrations. Froben Press, Inc., 1776 Broadway, New York 19, 1952.

The American Dermatological Association is the senior society of its kind in this country. Membership is by election and comprises, for the most part, teachers of dermatology and syphilology and outstanding practitioners. The bulk of this volume consists of a roster of the members, one page to each, with a biographic sketch and individual portrait—a veritable panorama of the leaders of the specialty from the beginning of the society to the present time. Honorary and Corresponding members, representing eminent and distinguished foreign contemporaries, are also listed. A few chapters are devoted to colorful reminiscences of the founders and charter members of the Association and incidents relating to the earlier scientific sessions.

Handbook of Tropical Dermatology and Medical Mycology. Edited by R. D. G. Ph. Simons, Amsterdam. Vol. 1. Price, $15., Pp. 845, with illustrations. Elsevier Press, 402 Lovett Blvd., Houston, Texas.

This is a very excellent collection of papers gathered together by Simons and numerous collaborators. The book deals with tropical dermatology and medical mycology, although there is considerably more of the former than of the latter. The photographs are excellent, and it is striking that so few typographical errors were encountered in the preparation of a book of this type. To those interested in tropical dermatology, the book is highly recommended.

Clinical Notes, New Instruments and Techniques

VITILIGO WITH A RAISED INFLAMMATORY BORDER

WILLIAM R. BUCKLEY, M.D.
AND
WALTER C. LOBITZ Jr., M.D.
HANOVER, N. H.

Vitiligo presenting a raised inflammatory border is rarely mentioned in dermatologic literature. The subject was recently reviewed thoroughly by Garb and Wise,[1] who at the same time presented a third case. The present report concerns a case which lately came under our observation.

REPORT OF A CASE

The patient was a 46-year-old white man, with chronic bronchial asthma, who had noted, over the period of one year, the development of a depigmented spot on the skin of the right anterolateral aspect of his neck. At first, during the next several months, the blanched area spread peripherally very slowly; it then increased rapidly in size, and, at the same time, similar areas appeared on the shoulders, chest, back, arms, and axillae. The only symptom associated with the depigmented areas was an occasional mild pruritus.

Physical examination of the skin showed several depigmented areas varying in size from 0.5 to 10 cm. in diameter (Fig. 1). The advancing border of the lesions was a slightly scaling, erythematous ridge with an elevation of 0.1 cm. (Fig. 2). The lesions were distributed as previously described.

Laboratory Data.—Direct examination of material from the lesions with potassium hydroxide repeatedly gave negative results. Cultures from lesions on Sabouraud's glucose agar were repeatedly negative. The Mazzini test for syphilis was negative. The red blood cell count and hemoglobin were normal. The white blood cell count was 7,700, with a differential of 51% polymorphonuclear leucocytes, 40% lymphocytes, 8% eosinophiles, and 1% monocytes. Urinalysis showed no abnormality.

Histopathology.—Tissue sections were fixed in formalin and stained with hematoxylin and eosin, silver nitrate, and periodic acid-Schiff stains. No fungus elements were revealed.

Histopathologic study of the tissue sections revealed a normally pigmented epidermis at one margin. This was abruptly continuous with epidermis showing mild spongiosis, marked liquefaction degeneration of its basal layer, occasional polymorphonuclear leucocytes, and a moderate diminution of pigment. This portion of the epidermis (the border of the lesion noted clinically) was continuous with the epidermis which showed a complete absence of pigment in its basal layer (the vitiligo noted clinically) (Fig. 3).

The cutis beneath the discrete area of spongiosis was heavily infiltrated with lymphocytes and pigment-laden macrophages (Fig. 4). The pigment was coarse and granular; it stained yellowish to dark brown with hematoxylin and eosin, and brown to black with silver nitrate.

Clinical Fellow in Dermatology, Dartmouth Medical School (Dr. Buckley).

From the Department of Dermatology and Syphilology, Dartmouth Medical School and Hitchcock Clinic (Dr. Lobitz).

1. Garb, J., and Wise, F.: Vitiligo with Raised Borders, Arch. Dermat. & Syph. **58**:149 (Aug.) 1948.

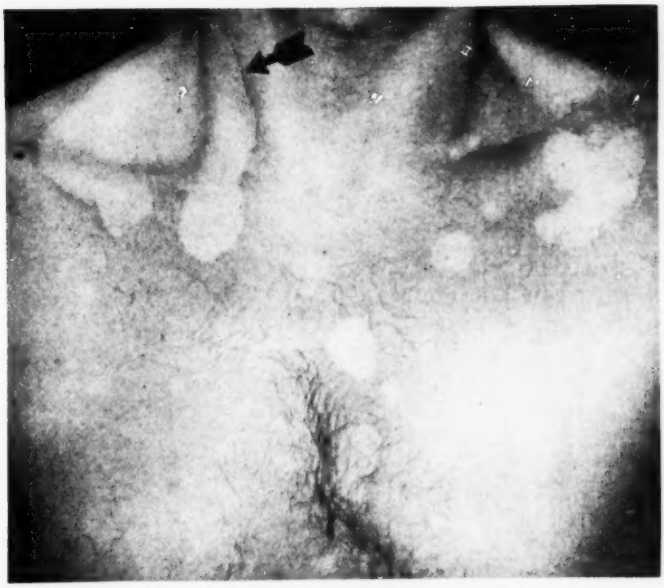


Fig. 1.—Vitiligo showing a raised border.

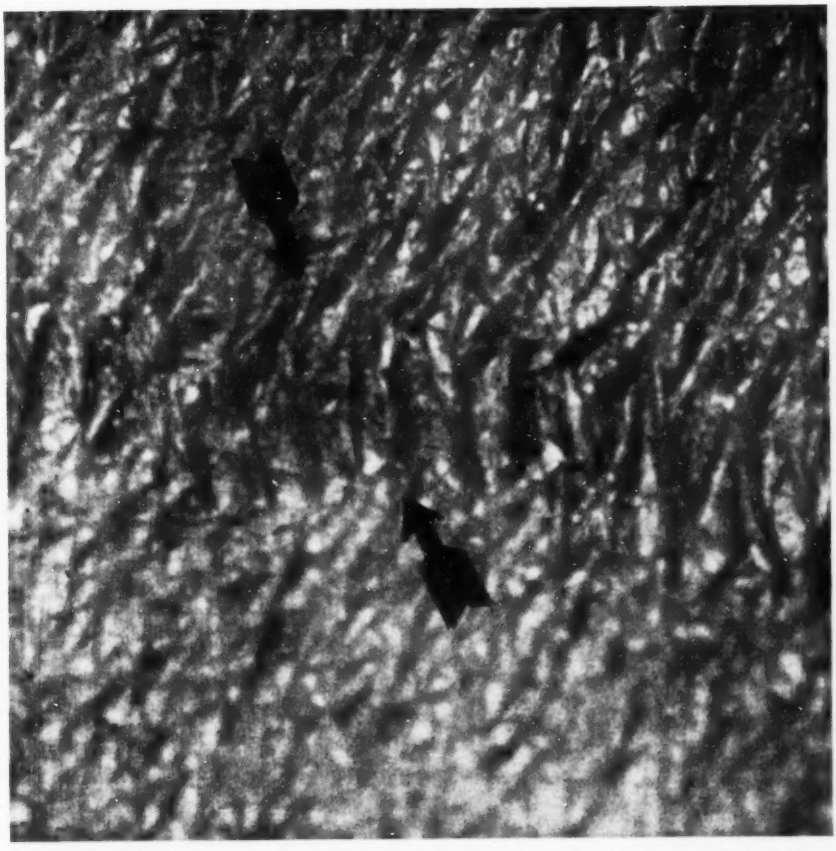


Fig. 2.—Slightly scaling, erythematous, elevated ridge. The advancing border of the lesion.

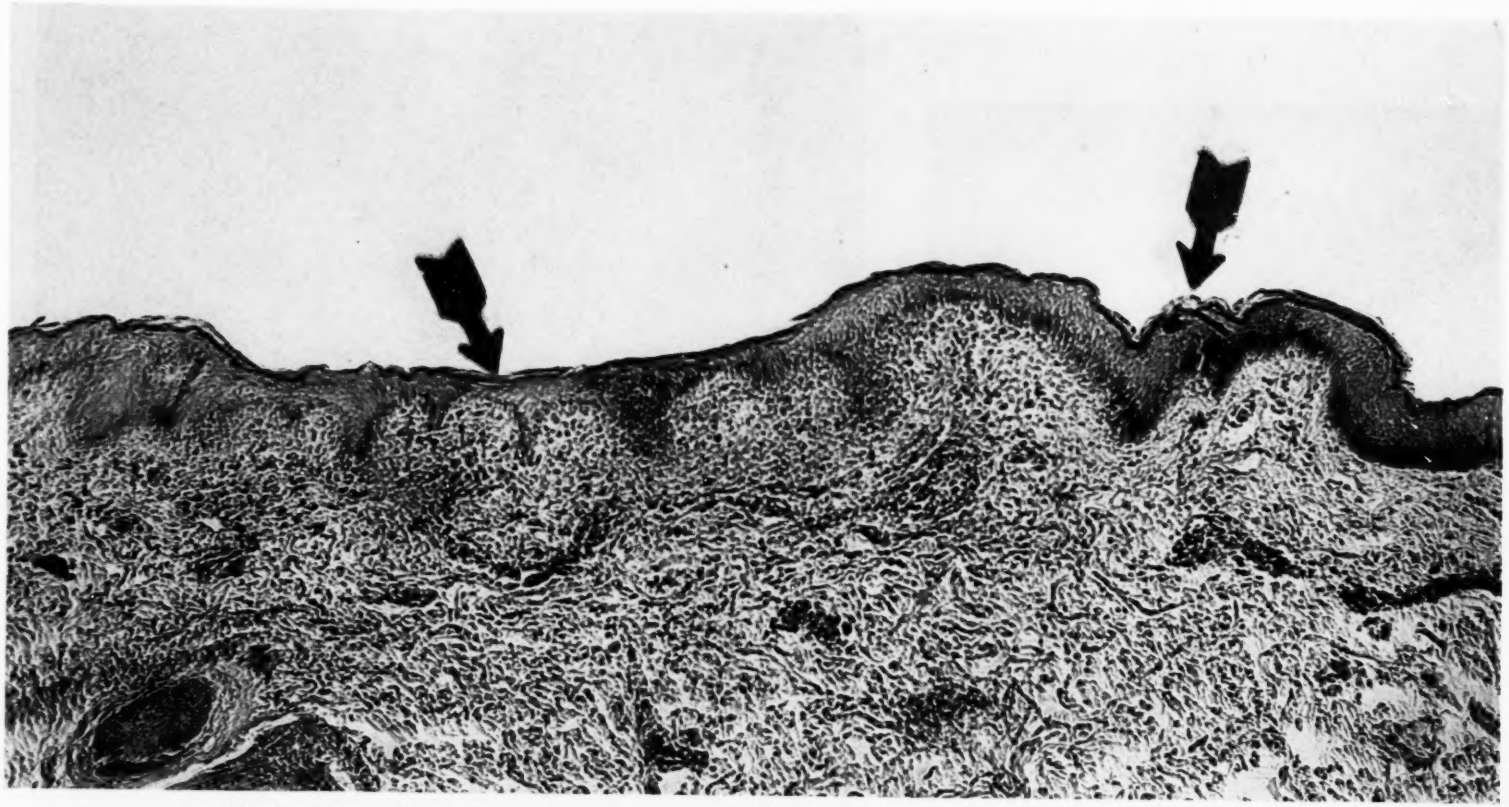


Fig. 3.—Arrows delineate the advancing border of the vitiligo; × 150. Tissue section stained with silver nitrate.

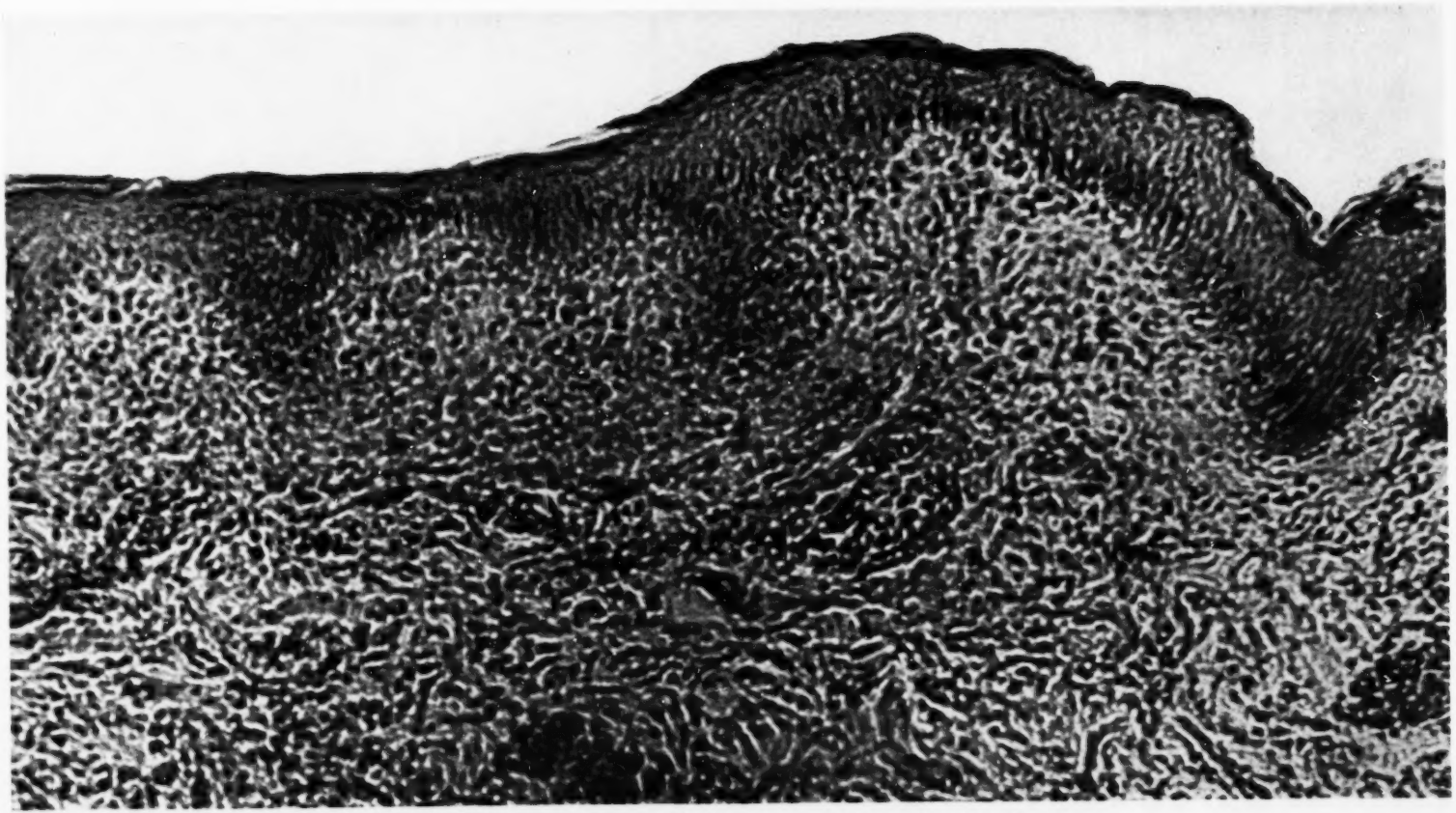


Fig. 4.—Delineated section; × 300. Tissue section stained with silver nitrate.

A smaller number of macrophages, described previously, were scattered throughout the middle and deeper cutis. The blood vessels in the superficial cutis were dilated. The sweat glands were surrounded by a mild lymphocytic infiltrate.

The cutis beneath the nonpigmented epidermis showed many scattered pigment-laden macrophages throughout its superficial portion and a smaller number in its middle and deeper portions.

COMMENT

In vitiligo, the exact cause of the disturbance of normal pigmentation is not known. The differential diagnosis of the lesions observed clinically included chloasma, contact dermatitis with secondary leucoderma, tinea versicolor, morphea, anesthetic lepra, partial albinismus, pinta, syphilis, achromia parasitica, and pellagra. Myxedema and hyperthyroidism were considered as general systemic conditions. All were ruled out as etiologic or contributing agents by the history, and by the clinical, laboratory, and histopathologic findings.

SUMMARY

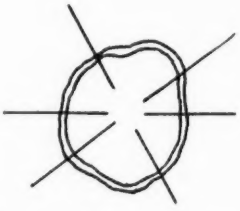
A case of vitiligo presenting a raised inflammatory border has been reported.

TREATMENT FOR GRANULOMA ANNULARE

HARRY M. ROBINSON Sr., M.D.
BALTIMORE

Granuloma annulare has not always responded satisfactorily to chemotherapeutic agents. Having noted as have others, that when pieces of tissue are excised for biopsy, the entire lesion, and others present, often will disappear, I considered it advisable to incise lesions (if scarring could be avoided) to note whether they would regress.

Two patients with granuloma annulare have now been treated in this way. Each lesion was wiped with alcohol and sprayed with ethyl chloride until snow appeared, and from four to six incisions were made through each lesion with a Bard-Parker pointed blade; these incisions



Incisions through lesion in granuloma annulare.

were not permitted to cross (Fig.). Even though one must cut deep enough to draw blood, healing is by first intention and without perceptible scarring. This procedure may be advisable when chemotherapy and x-rays fail, until a better treatment is found.

Of these two patients, A was a 15-year-old white girl, presenting one ringed lesion on the left hand. After two series of incisions, two weeks apart, the lesion completely regressed.

Patient B, a white boy 4 years of age, had eight lesions. Three of the lesions were incised by me every 10 days during three visits, and regressed by the end of that time; the remainder were incised every two weeks by the referring physician under my direction, and cleared up in four weeks. Although these lesions disappeared, two new ones appeared, one 1 mm. and the other 1 cm. in diameter; they also received incision treatment and involuted. No others appeared.

From the Department of Dermatology, School of Medicine and College of Physicians and Surgeons, University of Maryland.

Society Transactions

CHICAGO DERMATOLOGICAL SOCIETY

James R. Webster, M.D., President

Irene Neuhouser, M.D., Secretary

April 16, 1952

Rosacea with Severe Rosacea Keratoconjunctivitis for Twenty Years. Presented by invitation by Dr. Allan L. Lorincz.

A. K., a 59-year-old housewife, has had discomfort in the eyes associated with tearing and photophobia for the past 30 years. Flare-ups of eye discomfort have been associated with exacerbations of rosacea, which has been present over the face for more than 20 years. Examination of the eyes reveals corneal opacities, marginal corneal vascularization, and changes associated with chronic conjunctivitis such as conjunctival edema and inflammation, lacrimation, and trichiasis. There is a family history of similar disorder in the father and in at least one other of six siblings.

Results of general physical examination, except for papulopustular rosacea of the face and the eye changes, were essentially negative. Results of routine blood cell counts, urinalyses and Kahn tests have also been negative. Gastroscopic examination showed hypertrophic gastritis, and gastric analysis after histamine stimulation revealed complete achlorhydria.

The eye disease has resisted all therapeutic attemps to date, including superficial x-rays, large doses of riboflavin, and other vitamins administered both orally and parenterally, cortisone eye drops, diethylstilbestrol, and hydrochloric acid drops internally. The cutaneous rosacea has responded moderately well to Darier's paste (equal parts of zinc oxide, calcium carbonate, glycerin, and water) locally and routine rosacea management. Early rhinophyma, nevertheless, has been becoming evident during the past few years.

DISCUSSION

Dr. Stephen Rothman: There was a great initial enthusiasm among ophthalmologists about the therapeutic effect of riboflavin on rosacea keratitis. Slowly this enthusiasm faded away, and we know that rosacea keratitis is as intractable today as it ever was. I wonder whether anybody here has had experience with pyridoxine. There was a very encouraging report (*J. Lab. & Clin. Med.* **40**: 121 [July] 1952) on local application of pyridoxine ointments in seborrheic dermatitis after it was found that pyridoxine deficiency causes lesions resembling this condition.

Dr. Leon Goldman: Since studies on topical pyridoxine were initiated in Cincinnati, there has been considerable misunderstanding about the investigative nature of these reports. It was originally offered as an investigative study by Dr. Slinger and Dr. Vieter. Topical treatment with pyridoxine was used as an experimental procedure and not as a treatment for every form of severe seborrheic dermatitis. As a matter of fact, it aggravates the ordinary case of seborrheic dermatitis. The elderly person who is suffering with a noninflammatory seborrheic dermatitis around the hairline is helped by pyridoxine. No one has any idea about the stability of pyridoxine in ointment form.

Dr. Herbert Rattner: I have treated about six patients with pyridoxine ointment with favorable results up to a point—certainly no better than the results from sulfur ointment. What Dr. Goldman said should be emphasized, that this study may point to a new cause for certain diseases, namely, deprivation of vitamins, correctable only by topical applications.

Tuberculous Adenitis and Tuberculous Peritonitis. Presented by Dr. David Omens (by invitation), Dr. Harold Omens, and Dr. Stefan Bielinski.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: This is a good opportunity to discuss the change that is taking place in the treatment of tuberculosis. You all undoubtedly are aware of this change from physiological treatment to surgical treatment and now to chemical treatment. At the present time we have many drugs which are valuable, and some of them are almost dramatic in their effects. I have had the unique opportunity of treating two patients with the primary complex in the last two weeks. One patient was treated with streptomycin and paraaminosalicylic acid, and the ulcer healed very rapidly. In this patient the bacilli were easily demonstrated, and there was no question about the diagnosis. The first patient was a youth aged 18; in the second patient, about 35 years of age, who also had a primary ulcer, the organisms were demonstrated. To her we administered cotinazin® (isoniazid), and although the result was not as dramatic as in the previous case, it was marked enough to lead us to believe that the drug is effective. The adenitis in both cases was not unlike that seen in the groin of the presenting patient. I spoke to Dr. Tucker, who is in charge of the tuberculosis service at our Veterans' Hospital; he agreed that the treatment of tuberculous adenitis is very hard to outline. I told him that I was going to use the chemical treatment for a while and that if the adenitis did not subside I would recommend surgical removal, not x-ray treatment. Since tuberculous adenitis can be controlled with a fair degree of success, surgical removal in the resistant cases seems to be more satisfactory than radiation.

About the peritonitis, I have had no experience except that I have seen patients with tuberculous peritonitis and I was told by the men in charge that this was one form of tuberculosis which responded well to x-ray therapy. I think a consultation with that in mind would be advisable.

DR. A. M. BUCHHOLZ: I, too, would like to contribute a little experience, which has not been published as yet, on the use of isonicotinic acid in scrofuloderma. The series is small, and these cases of adenitis, as Dr. Michelson pointed out, are rather resistant to treatment. Under control conditions the few cases submitted to this therapy seemed to melt away. Of those cases in which the disease did not disappear completely in 50% there seemed to be improvement. It is also to be noted that afterward in some of these cases when the disease is refractory we find some tuberculosis bacilli but not as many as before. When we subject these bacilli to pathogenic tests we find that their virulence has decreased. Whether this will continue to be true in the future or whether resistance will develop remains to be seen.

Leprosy. Presented by DR. M. H. EBERT and (by invitation) DR. B. YAFFE.

C. E., a 26-year-old Mexican man, was first seen two days ago in the Skin Clinic of the Central Free Dispensary. He has had a generalized eruption of short duration. Because of language difficulties and the schizoid attitude of this patient, an accurate history was not obtainable.

He has been living with a group of young Mexican émigrés and working as a punch press operator for about one year in the United States. Three years ago in México, D. F., he was given shock therapy for schizophrenia.

Examination revealed a young, asthenic man who is partially cooperative but retarded in speech and motor activity. Contact with environment is detached and catatonic positions can be induced. Over the posterior aspects of both arms and buttocks are many discrete, pea-sized, bluish-red nodules. The overlying skin is natural, a varnished or oiled surface is suggested, and on palpation the lesions are normal in consistency. Sensory changes to temperature and pin prick are indeterminate. Both lower extremities are similarly involved, and eczematoid changes are present about the ankles.

A biopsy specimen is presented from a cutaneous nodule.

DISCUSSION

DR. IRENE NEUHAUSER: I believe this is a case of leprosy of the type described by Lucio. There is a diffuse flushing of the face with telangiectasis. On the lower extremities there are a number of erythematous, slightly infiltrated macules with central crusts, and a lesion with central vesiculation on the left knee. A biopsy specimen of the lesion on the leg would probably show vasculitis. The patient comes from Aguascalientes, which is near the state of Sinoloa, where

many cases of this diffuse type are found. The patient states that these lesions have been present for only three weeks. There is no doubt that this is a very early case. Although the biopsy shows lepromatous leprosy, there is no alopecia or thickening of the eyebrows or ear lobes. This is a malignant type of leprosy, and the patient should be isolated.

DR. LEON GOLDMAN, Cincinnati: As Dr. Neuhauser did, I made the diagnosis after I looked at the biopsy specimen. Those of us who are untrained leprologists have to think of the association of sensory difficulties with a local skin lesion. In a patient of that type your only recourse when you cannot gain cooperation is to attempt to do a histamine test, and you might later try with your neurological department to see whether you can pick up associated nerve difficulties with electrical resistance studies. This man has the Lucio type, which is the necrotizing vasculitis type, of lepromatous leprosy. On the arms there was no evidence of very much save folliculitis. Dr. Neuhauser is perfectly right that a biopsy should be done on some of these lesions on the leg. These lesions on the face look like nevi, but he says that they have been present only three weeks (?), so they must be part of the lepromatous leprosy. Because the Lucio type is a "Mexican" variety, it is not surprising that you find it wherever you find these migrant Mexicans.

DR. STEPHEN ROTHMAN: I should like to recommend the pilomotor nicotine test to examine peripheral nerve degeneration. This test is extremely sensitive and easier to interpret than the histamine test (Arnold, H. L., Jr.: *Internat. J. Leprosy* **16:** 335-346, 1948).

DR. NEUHAUSER: In the diffuse type of leprosy the organism is usually found in any region of the skin. The scraped incision method should be done. The organism should be found in large numbers.

DR. A. M. BUCHHOLZ: We know that the response of the tuberculosis bacillus to isonicotinic acid is very good. We know that it is a Gram-negative bacillus, and so is Hansen's bacillus. There is much favorable laboratory evidence that this drug will be helpful in leprosy. I just bring this up so that the presenters may watch it and see what it will do in this patient.

A Case for Diagnosis. Presented by DR. ALFRED B. FALK, and (by invitation) DR. FRANCIS HETREED.

K. D., aged 16 months, first had a scanty papular eruption on her right arm in October, 1951. New lesions appeared on the legs, face, and arms, while a few of the old ones would involute spontaneously over a period of several months. Itching is minimal. The past history was negative. No insects have been found at home. No one else in the home has any rash. The patient was hospitalized for study.

Findings at general physical examination were negative.

In February, 1952, a biopsy was done of one of the papules on the leg. The essential findings were in the dermis, consisting of nests of round cells containing large pale reticulum cells and eosinophiles. At the layer of subcutaneous fat many more eosinophiles were seen. Special stains of elastic tissue were essentially normal.

Laboratory data were as follows: nonprotein nitrogen 39 mg. and urea 16 mg. per 100 cc. of blood; cephalin flocculation test, ++; cholesterol 238 mg. and calcium 12.4 mg. per 100 cc. Results of serologic and Mantoux tests, of urinalysis, and of bone marrow study were negative. There were 4,720,000 red blood cells. Hemoglobin was 11 gm. per 100 cc. There were 8,200 white blood cells, with neutrophiles 54%, basophiles 1%, lymphocytes 25%, and monocytes 9%; the rest of the white blood cells were stab cells, young cells, and toxic lymphocytes.

X-rays of chest, skull, and pelvis were negative.

DISCUSSION

DR. LEON GOLDMAN, Cincinnati: I think that clinically the one primary lesion that this child has is suggestive of lichen urticatus. The biopsy specimen is also characteristic of the type of nonspecific reaction that we see in lichen urticatus. There are different forms of lichen urticatus. The seasonal variety, especially in the person without atopy, is related usually to a type of hypersensitivity to the bites of various arthropods.

DR. F. E. SENEAR: Does Dr. Goldman still distinguish lichen urticatus as such, or does he believe that all cases are due to insect bites?

DR. GOLDMAN: I have never proved that the chronic form of lichen urticatus is due to arthropod bite sensitivity.

DR. THEODORE CORNBLEET: I am not sure that the proponents of the insect-bite-etiology theory of lichen urticatus allow for other causes. We believe that there are cases in which insects are not at fault and which will respond to treatment without regard to such possible intervention.

DR. GOLDMAN: Lichen urticatus is just a morphological type of hypersensitivity reaction. It is not an etiologic diagnosis. The acute type, which occurs occasionally and which is related to arthropod bite, usually can be found associated with local arthropod bite reaction. So-called chronic lichen urticatus, especially in a person with atopy, is as confusing and disturbing to me as is atopic dermatitis.

DR. MALCOLM C. SPENCER, Danville, Ill.: The majority of cases of papular urticaria reported by us (*J. Invest. Dermat.* **11**: 293-298 [Oct.] 1948) were found to be caused by sensitivity to insects. In most cases, insect sensitivity was demonstrated to Cimex or fleas, although in some cases sensitivity to mosquitoes was felt to be the cause of the eruption. Presumptive evidence for this thesis of insect allergy as a cause of papular urticaria was obtained by reviewing the histories of cases seen in the clinics of the hospital of the University of Pennsylvania group over the past ten years. It was found that an overwhelming majority of cases were seen during the warm weather months at the time when insect activity is at its height. Furthermore, a careful history of the cases presented reveals that a significant number of the patients were exposed to sources of these insects, either directly in the home or from pets, sand boxes, etc. It was also noted that the incidence of papular urticaria declined quite significantly with the general use of chlorophenothane (DDT) as a household spray. It was felt by many observers that the incidence, for example, at the Children's Hospital had dropped at least 75%. Antigens made from Cimex and fleas used for testing sensitivity were found to elicit positive tuberculin-like reactions in a significant number of cases studied. Furthermore, the therapeutic response with a shake lotion or a plain powder containing 5% chlorophenothane reduced the course of the eruption by several weeks when compared with the previous treatments used for papular urticaria.

Enteropathic Acrodermatitis (Danbolt): Successful Treatment with Diodoquin® (Diiodohydroxyquinoline). Presented by DR. CALVIN J. DILLAHA (by invitation) and DR. ALLAN L. LORINCZ (by invitation).

B. C., a 3-year-old girl, was first presented before the Chicago Dermatological Society in October, 1951, with the incorrect diagnosis of dystrophic epidermolysis bullosa. In the discussion of this patient at that time Dr. S. W. Becker suggested that this was a case of systemic moniliasis. Dr. Herman Pinkus suggested that the clinical picture in this patient closely resembled that in three cases described by Danbolt (*Acta dermat.-venereol.* **23**:127, 1943).

Since 2 months of age this patient has suffered from a recurrent vesicular, erythematous, crusted dermatitis involving the forehead, cheeks, perioral area, elbows, hands, sides of the fingers, paronychial areas, heels, ankles, the inner aspect of the thighs, the knees, buttocks, and perianal region. A complete alopecia occurred at 5 months of age. Then there was a period of complete remission lasting three months at 1 year of age.

After the first presentation, Candida albicans was cultured from a number of lesions. However, after a period of therapy with Castellani's paint all cultures were free of the organism; they have remained so in spite of the fact that vesicular lesions continued to occur at areas of previous involvement.

Hospitalization and nonspecific therapy usually resulted in gradual improvement in the skin lesions over a period of several weeks. A similar gradual improvement followed a course of orally given cortisone acetate (50 mg. daily for one week, 37 mg. daily for three weeks). At the conclusion of the latter therapy, there was also noted a beginning regrowth of scalp hair, eyelashes, and eyebrows. Shortly after cessation of this therapy, vesicular lesions appeared at the sites of all previous lesions and the hair began to fall out.

In retrospect it was noted that during the periods of relative quiescence of the disease the patient had only one to two well-formed stools daily, while during the periods when the disease was active, the stools were loose, and four to six daily.

Following the last flare-up the patient received gantrisin* (sulfisoxazole), 0.5 gm. four times a day, without benefit for one week.

The administration of diodoquin* (diiodohydroxyquinoline), 210 mg. four times a day, was followed in four days by a rapid resolution of all skin lesions and by the regrowth of hair. Administration of the latter drug has been continued since initiation one month ago. The stools are now well formed, one to two daily.

Further studies of the stools and immunologic reactions of the patient are now in progress.

DISCUSSION

DR. STURE A. M. JOHNSON, Madison, Wis.: The patient appears to be well at this time. The photographs suggest a severe infection due to C. albicans. The response to diiodohydroxyquinoline does not rule out moniliasis, since we have had good results with the drug given orally in two children with C. albicans infection of the scalp, nails, genitalia, and gastrointestinal tract. These two cases paralleled the clinical picture of the patient presented today.

A, bullous and erythematous lesions of the lower extremities; *B*, clearing of lesions after one week of therapy with diiodohydroxyquinoline; *C*, continued improvement after one month of therapy with diiodohydroxyquinoline.

DR. CALVIN J. DILLAHA (by invitation): In studying this patient, we have gone through the literature and have found 20 cases with this identical clinical picture. The disease has been variously described as dystrophic epidermolysis bullosa, systemic moniliasis, acrodermatitis continua, and dermatitis with gastrointestinal disturbances. All these patients have several things in common: (1) total alopecia; (2) skin lesions with localization around the body orifices and on the extremities, and (3) diarrhea or other obscure gastrointestinal dysfunctions; frequently the disease was fatal.

In some of the cases in the literature C. albicans has been demonstrated in the skin lesions, and because of the widespread lesions the disease was called systemic moniliasis. We found C. albicans organisms in our patient; they responded, however, to local therapy with Castellani's paint. After this the skin lesions on repeated culture were free of yeast, and yet new lesions continued to appear.

Danbolt (*Acta dermat.-venereol.* **23**:127, 1942; **28**:453, 1948) emphasizes that this disease may have its onset when breast feedings are discontinued. In several of his cases he produced remissions by feeding breast milk. These remissions lasted only so long as breast milk was given.

DR. ALLAN L. LORINCZ (by invitation): An additional point about this disease is that on occasion it has occurred in several siblings of the same family. This familial tendency was

pointed out by Danbolt (*Acta dermat.-venerol.* **28**:540, 1948). As concerns the rationale of diiodohydroxyquinoline therapy in this disease, I can only say at this time that it is entirely empirical. Dr. Elias Schlomovitz, of Milwaukee, discussed with me a case diagnosed as systemic moniliasis, which he treated very successfully in this manner. I was struck by the similarity of his case to ours and decided to try diiodohydroxyquinoline. This treatment certainly also succeeded very dramatically in our patient.

Bullous Eruption—Pemphigus? Presented by DR. HERBERT RATTNER, DR. HAROLD RODIN (by invitation) and DR. J. F. SICKLEY.

Hyperpigmentation (Sarcoidosis?). Presented by DR. THEODORE CORNBLEET, DR. DAVID COHEN (by invitation), and DR. J. F. SICKLEY.

Porphyria Pigmentation. Presented by DR. HERBERT RATTNER, DR. HAROLD RODIN (by invitation), and DR. STEFAN BIELINSKI.

Keratosis Pilaris? Lichen Spinulosis? Presented by DR. THEODORE CORNBLEET, DR. DAVID COHEN (by invitation), and DR. STEFAN BIELINSKI.

Scleroderma? Presented by DR. HERBERT RATTNER, DR. HAROLD RODIN (by invitation), and DR. STEFAN BIELINSKI.

Linear Scleroderma. Presented by DR. MALCOLM C. SPENCER.

Pityriasis Lichenoides et Varioliformis Acuta (Haberman). Presented by DR. STANLEY HUFF and (by invitation) DR. B. J. PASS.

Nodular Nonsuppurative Panniculitis. Presented by DR. RICHARD M. OLIVER.

Intraepidermal Epithelioma. Presented by DR. A. W. STILLIANS.

Xanthoma Palpebrarum with Involvement of Conjunctiva and Xanthosis of the Neck, Chest, and Arms. Presented by DR. SAMUEL J. ZAKON and DR. M. J. BARRASH (by invitation).

Tertiary Syphiloderm. Presented by DR. M. H. Ebert and (by invitation) DR. B. YAFFE.

Pustular Psoriasis vs. Acrodermatitis Continua of Hallopeau. Presented by DR. F. E. SENEAR and DR. M. J. BRUNNER.

Nevoxanthoendothelioma. Presented by DR. MALCOLM C. SPENCER.

A Case for Diagnosis (Sarcoid?). Presented by DR. MARCUS R. CARO.

Pseudopelade (Alopecia Cicatrisata). Presented by DR. MARCUS R. CARO and DR. LOUISE E. TAVS.

Multiple Idiopathic Hemorrhagic Sarcoma (Kaposi): Single Lesion for Twenty-Five Years. Presented by DR. A. L. SHAPIRO.

Keratosis Palmaris et Plantaris (in Its Early Stages). Presented by DR. EDWARD A. OLIVER.

MANHATTAN DERMATOLOGIC SOCIETY

Samuel M. Peck, M.D., *President*

George M. Lewis, M.D., *Secretary*

April 8, 1952

Leucotrichia. Presented by DR. NATHAN SOBEL.

H. S., a boy aged 11, was first seen on March 19, 1952, at the Skin and Cancer Unit. About five months ago he noticed a loss of color of some of the eyelashes of the left upper and lower lids, the black color changing to snow-white. Within a period of two months all the eyelashes except two on these lids had become white. During the past two weeks a number of depigmented hairs have appeared at the inner end of the left eyebrow. The skin and hair elsewhere appear normal. There is no history of preceding local dermatitis of the eyelids and no previous illnesses except measles and chicken pox in 1950. The parents and younger sister have no pigmentary disorder.

DISCUSSION

DR. WILBERT SACHS: The interesting part to me is that the intervening skin remains normal. I can't understand how the disorder can affect the hair and not the skin in between.

DR. DAVID BLOOM: My concept is that it is like vitiligo of the skin, and there is no explanation of why just the hair should be affected. I have seen such a disorder in one boy, and I don't know whether it was in spite of treatment or because of it, but after treatment with vitamin B and paraaminobenzoic acid the pigment returned. It might return without any treatment whatsoever in this case, since the patient has had the condition only a few months.

DR. FRANK C. COMBES: I don't know how much you can do about it. We do hear about gray hairs responding to pyridoxine hydrochloride and paraaminobenzoic acid. I agree with Dr Sachs that it is interesting to have the intervening skin clear. The other patient presented tonight had loss of pigment only in the skin and not in the hair.

DR. FRANK E. CORMIA: I am interested in Dr. Bloom's remarks. I recall a few elderly patients I have had with seborrheic dermatitis to whom I gave vitamin B complex. After a period of two or three months the hair darkened appreciably. Whether that would help this boy, I don't know.

DR. THOMAS N. GRAHAM: I presented this patient at the Metropolitan Dermatological Society or at the New York Academy of Medicine. I think he has vitiligo, and nobody knows the cause of that. I don't think there is anything you can do in the way of treatment. You have to wait and see what will happen. I suggested the use of mascara to the family.

DR. ORLANDO CANIZARES: I wonder whether it could be a type of nevoid change. We know that there is some effect on degrees of pigment.

DR. NATHAN SOBEL: I presented this case as an oddity, because I have seen very few cases in which the eyelashes alone were involved. As far as treatment is concerned, I have never ordered anything but a disguising application such as "covermark." I think mascara is an excellent suggestion.

Urticaria Pigmentosa. Presented by DR. ORLANDO CANIZARES.

M. H., a woman aged 39, is presented from Bellevue Hospital with a generalized eruption of 21 years' duration. The onset was gradual, the eruption appearing first on the chest and gradually extending to the rest of the body. The eruption has remained unchanged in spite of many kinds of treatment. The patient was previously presented before the New York Academy of Medicine by Dr. Bloom, about 12 years ago.

The patient has lost weight during the last few years. At present she weighs 98 lb. (44.5 kg.) and her height is 5 ft. 4½ in. (163.83 cm.). She complains of occasional gastric disturbances, but all laboratory examinations have given normal results. She has been told she has a "nervous stomach." In recent years the patient has been much concerned with her skin condition and has become very nervous.

There is a generalized eruption involving chiefly the trunk and extremities. The face is involved only on the cheeks. The lesions are macules and slightly elevated papules. The macular lesions are profuse and erythematous and present many telangiectases. They tend to coalesce and present a retiform distribution. The elevated lesions, mainly on the upper extremities, are skin-colored. When rubbed, the lesions become red and swollen.

The Wassermann reaction of the blood was negative. A biopsy specimen in 1940 was said to be consistent with the diagnosis of urticaria pigmentosa. Another biopsy specimen, taken on April 2, 1952, has not been reported on as yet.

DISCUSSION

DR. THOMAS N. GRAHAM: I couldn't quite agree with the pigmentosa part of the diagnosis. However, I think the biopsy proved it. I would agree with the diagnosis.

DR. ANTHONY C. CIPOLLARO: I don't know what the pigment is here. If it is urticaria pigmentosa, it is an unusual manifestation of that disease. Looking at it from a distance, one gets the impression that one is dealing with poikiloderma, but on closer inspection there is absence of atrophy and areas of pigmentation. I would suggest that another biopsy be performed. One biopsy some years ago indicated that the patient had urticaria pigmentosa. I have no diagnosis to offer.

DR. PERRY SACHS: With the patient's continued loss of weight and the telangiectasis purpura element, I think some systemic disorder should be sought. Furthermore, she claims that she is much worse in winter; I believe cryoglobulin investigations should be made.

DR. MAURICE J. COSTELLO: I have seen telangiectases develop in patients with long-standing urticaria pigmentosa, but I have never seen it in such extensive lesions. I think, as Dr. Sachs said, that the patient has lost much weight and should have a general physical examination to determine whether there is anything else wrong.

DR. WILBERT SACHS: Clinically, I wouldn't be able to make a diagnosis of urticaria pigmentosa. I have never seen such telangiectases in that disease.

DR. GEORGE M. LEWIS: I have never seen anything like this as a manifestation of urticaria pigmentosa, and I am sure another disease must be present, even if she has urticaria pigmentosa. I agree with those who think she should be studied for some internal disorder. This should include the hemopoietic system in particular.

DR. NATHAN SOBEL: I agree that the patient should be studied for some systemic disease, but I should remind the members that Parkes Weber described a type of urticaria pigmentosa in which the characteristic feature was telangiectasis and redness of some of the lesions.

DR. DAVID BLOOM: It must be 14 years ago that I presented this patient from Bellevue Hospital, at the New York Academy of Medicine. At that time she weighed about 60 lb. (27.2 kg.) more than she does now. I would not have recognized her. I think this is a type of urticaria, as Dr. Sobel has suggested.

DR. FRANK C. COMBES: I agree with everything Dr. Lewis has said.

DR. FRANK E. CORMIA: In this disease, presumably when the skin is injured or traumatized, histamine is liberated from these abnormal cells. One wonders whether there would be an abnormal reaction to the histamine which is manifesting itself.

Case for Diagnosis: Erythema Annulare Centrifugum? Erythema Multiforme? Erythema Elevatum Diutinum? Granuloma Annulare? Presented by DR. THOMAS N. GRAHAM.

Pemphigus Vulgaris Complicated by Diabetes, Successfully Treated with Corticotropin (ACTH) and Cortisone. Presented by DR. DAVID BLOOM.

Dermatitis Medicamentosa. Presented by DR. THOMAS N. GRAHAM.

Peculiar Pigmentation and Depigmentation of the Skin. Vitiligo? Presented by DR. ORLANDO CANIZARES.

Case for Diagnosis: Atopic Eczema? Prurigo? Presented by DR. GEORGE M. LEWIS.

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Dec. 5, 1951

Traumatic Hemangioma. Presented by DR. BERNARD APPEL, Lynn, Mass.

M. C., a 14-year-old girl, was kicked in the right shin two years ago. After the injury, a black-and-blue swelling appeared. After several weeks the swelling assumed a pinkish-red color, which has persisted since. There is intermittent throbbing pain in the lesion.

On the anterior aspect of the right leg overlying the tibia 8 cm. above the ankle joint, there is a dull pinkish-red somewhat tender swelling measuring 5 cm. by 6 cm. The lesion appears to be in both skin and subcutaneous tissue.

The x-ray of the right leg showed nothing significant, both at the time of the original injury and one and one-half years later.

DISCUSSION

DR. FRANCIS P. MCCARTHY, Boston: In what way will trauma produce a tumor made up of blood vessels? In the light of the number of traumatic lesions suffered during a lifetime and the many millions of people who undergo such trauma, the rarity of such tumors is noteworthy. There is a possibility that there was a tumor present before the trauma. It would be interesting to dissect out this lesion and examine it microscopically to try to discover how a hemangioma develops following an injury. This lesion blanches on pressure. It is a hemangioma clinically. Possibly the patient might be willing to have the lesion excised, especially since she is having symptoms of pain and discomfort.

DR. E. MYLES STANDISH, Hartford, Conn.: We should consider an arteriovenous aneurysm, although one cannot feel pulsation in the tumor.

DR. NEVILLE KIRSCH, Hartford, Conn.: I think the lesion ought to be excised first. I do not know exactly how deep it is. It may develop into an arteriovenous aneurysm. I did not feel pulsation, either.

DR. JOHN G. DOWNING, Boston: I believe that blood vessel tumors can result from trauma. Several years ago, I wrote a paper on hemangioendothelioblastoma as a result of trauma. I followed these cases and similar cases a number of years ago. One patient had a hemangiomatous lesion on his one good leg, the other leg having been lost in an accident. It was decided to remove that lesion from the remaining leg. As a result of that operation, the patient then had a series of hemangiomatous lesions extending up the leg.

There is no question in my mind that hemangiomatous lesions can result from trauma. Every one of us now and then sees a nevus araneus which results from picking or squeezing. The more conservative the treatment, the less cause for regret.

DR. BERNARD APPEL, Lynn, Mass.: In a case of this sort, treatment depends to a large extent on the psychological approach that the doctor has to the problem. If the doctor should happen to be a scientific enthusiast, I think there is a reasonable probability that in this little girl some kind of deformity would eventually develop. I cannot conceive of attempting a surgical procedure on this lesion, unless one is prepared to do a rather wide and extensive resection. I feel that it is probably not an aneurysm. If it were, it would be much bluer than it is. Its color and its lack of pulsation point more toward a hemangioma rather than arteriovenous aneurysm. If that lesion were located, e. g., on the buttocks or the upper posterior thigh, and if it were important to make the diagnosis, then one might consider surgery, but I would not recommend surgery in this location.

Nevus Sebaceous(?) Presented by DR. WILLIAM HALPERN, Worcester, Mass.

M. P., a 60-year-old Italian-American laborer, is known to have had an asymptomatic lesion on the back for 33 years. The patient was treated for syphilis 20 years ago.

On the left posterior chest there is an irregular raised pinkish-yellow slightly nodular lesion about 4 cm. by 7 cm. There is a soft pink pedunculated tumor arising from the center of the lesion.

Serologic reactions for syphilis were negative. Two biopsies from the lesion have been reported to show normal skin.

DISCUSSION

DR. ALFRED HOLLANDER, Springfield, Mass.: The problem of interest in this case concerns classification. Although I feel that there are certain sebaceous elements in the lesion, I think it consists mainly of fibrous tissue.

DR. BERNARD APPEL, Lynn, Mass.: Although it is reported here that the biopsies show normal skin—and I must admit that I accepted that—on reexamining those slides today I think even although the epidermis might be normal the entire skin is not normal, because there is an extremely large amount of loose, fibromatous tissue subepidermally, extending to the bottom of the biopsy specimen. I think this is a fibromatous type of lesion. It may be a nevus type of soft fibroma, or it may be merely a mass of spontaneously developing soft fibromata.

DR. WILLIAM HALPERN, Worcester, Mass.: This patient was presented because clinically we made a diagnosis of nevus sebaceus. When we first examined the slides, we thought the skin was fairly normal. The surprising fact is that a relatively normal biopsy came from this lesion.

Chronic Disseminated Lupus Erythematosus. Presented by DR. WILLIAM WOLF, Lowell, Mass.

M. F., a 47-year-old white housewife, had a skin lesion on the right upper arm one year ago. The lesion disappeared in response to corticotropin (ACTH) therapy, given for arthritis, only to reappear three weeks after the cessation of steroid therapy. In June, 1951, after she had been sitting in the sun, a much more extensive eruption developed.

Examination reveals irregular patches of erythema and slight scaling on the extensor aspect of the arms and on the neck and central area of the chest. Atrophy and follicular plugging are present in the periphery of the larger plaques on the forearms. Lesions are present in the scalp, but there is no alopecia.

White blood cell counts have varied between 3,500 and 8,200. Biopsy shows a picture which was considered to be typical for an acute lupus erythematosus.

DISCUSSION

DR. JOSEPH GOODMAN, Boston: I look on this patient as having a rather serious and dangerous form of lupus erythematosus. The classification of this particular type is difficult, but I believe the proper diagnosis is subacute lupus erythematosus. This is not an acute disseminated lupus erythematosus, although certain features of the clinical picture, such as arthritis, and leucopenia, fit that diagnosis. The lesions themselves present features which suggest chronic discoid lupus erythematosus.

Since I have had occasion to follow the cases of two patients with similar eruptions to a fatal termination, I have begun to look on this type, with involvement of the V of the neck and of the arms, as a serious one, even without a low white blood cell count, without arthritis, and without lesions on the fingers.

Patients who present this clinical picture do not have true discoid lupus erythematosus or true acute disseminated lupus erythematosus. I have never seen this type of eruption develop in a patient who had a discoid lesion over a period of years. Patients in whom this picture develops may have facial lesions alone, but they have lesions on the arms, chest, and elsewhere relatively soon after their first lesion develops, and not years later.

DR. E. MYLES STANDISH, Hartford, Conn.: The case of this woman is almost an exact counterpart of that of a patient seen at the Hartford Hospital in November, 1950. A year or two previously she had arthritis and was told to sit in the sun. At that time, she had one or two skin lesions. Immediately there was a general distribution of the lupus erythematosus, much like that of the patient presented today, but at no time was the process really acute. She was not very sick when she went into the hospital. She had a high sedimentation rate. With cortisone therapy she felt better almost immediately, but objectively she was not much changed. After five weeks in the hospital, we found that she could not get along with less than 100 mg. of cortisone a day. She is still taking cortisone, so far as I am aware. I believe that it would have been better for her if cortisone therapy had not been started.

DR. MAURICE M. TOLMAN, Boston: It is interesting to get drawn into this type of discussion, to have the opportunity to go back over 20 years, and to follow some of these cases from a time when we thought we knew some of the answers to a time when we know almost nothing. We do not agree on the names. We are dealing with a condition of discoid lupus erythematosus, or we are dealing with a disease which is a systemic condition, which may or may not be accompanied by skin lesions. It is no longer a question of whether in a given case discoid lupus erythematosus may or may not disseminate within a period of years or whether in the process of disseminating there is a so-called subacute picture.

Some time ago, when we first became interested in this problem, the chief type of case we saw was, of course, discoid lupus erythematosus, and the so-called disseminate type was one that occurred undiagnosed in the medical wards. Then wire loop pathology was described. Sachs and Libman published their findings; then fluid was found in the cavities, and a change was found in globulins with a positive serologic reaction for syphilis related to the globulin. In the course of therapy we find the same situation. In discoid lupus erythematosus, whether we use bismuth or gold or calcium gluconate, or arsenic by mouth, a certain percentage of patients with discoid lesions recover and remain completely free of lesions for a period of time. No matter what we use, the lesions recur in a certain percentage. The situation is the same with regard to the use of cortisone, whether by mouth, under the skin, in the skin, or in the muscle. The previous therapies have all proved to be nonspecific, and I am sure the same will be found to be true of cortisone, at least in reference to the discoid type.

Why lupus erythematosus should in one instance become complicated by dermatomyositis, scleroderma, poikiloderma, or any combination of them and then in another instance remain localized is something which we may in the future be in a position to explain. From observation, it is my firm belief that these various types of reactions represent cellular responses to trauma and infection.

Fibrosarcoma. Presented by DR. FRANCIS P. MCCARTHY, Boston.

M. B., a 9-year-old boy, had a small nodule at the angle of the right scapula about one year ago. Several additional nodules have appeared in the vicinity of the original lesion, the last one having been noticed two months before presentation. There has been no pain or discomfort in the lesions.

In an area measuring about 8 cm. by 3 cm. on the right back just below the scapula, there are 10 nodules. Each is about 2 cm. in diameter, slightly raised, and bluish-red. Each nodule is hard, movable, and nontender.

Biopsy reveals fibrosarcoma.

DISCUSSION

DR. BERNARD APPEL, Lynn, Mass.: I should like to suggest that in this case a certain form of surgery is indicated. We are all aware of the dangers of doing an ordinary surgical dissection for this type of lesion. If that were done, there is a reasonable expectation that shortly thereafter there would be more lesions.

It seems to me that Moh's chemosurgery would be appropriate here, because the lesion could be destroyed with continual histologic control. Subsequently, plastic restoration should not be too difficult to do.

DR. ALFRED HOLLANDER, Springfield, Mass.: I do not believe that Moh's therapy is indicated in this case. The treatment of choice is excision followed by a plastic repair.

DR. FRANCIS P. MCCARTHY, Boston: Over a lifetime, I have seen fibrosarcomata removed from adults along the lines Dr. Appel has indicated. Six months or a year later, another specimen is received from the same site. Then a year or two later, there is another specimen. I have followed one case in which there were repeated dissections over a period of 20 years. All the specimens showed fibrosarcomata.

I should like to believe that this is a benign lesion, but because of the clinical course and the microscopic picture I do not think it is. The surgery done in the past on such cases has not been radical enough.

Chronic Radiodermatitis, Basal Cell Epithelioma. Presented by DR. BERNARD APPEL, Lynn, Mass.
Epithelial Cysts, Resembling Basal Cell Epitheliomata. Presented by DR. BERNARD APPEL, Lynn, Mass.
Sclerosis Basal Cell Epithelioma. Presented by DR. BERNARD APPEL, Lynn, Mass.
Chronic Discoid Lupus Erythematosus. Presented by DR. MAURAY J. TYE, Haverhill, Mass.
Neurotic Excoriations? Macular Atrophy Secondary to Varicella? Presented by DR. BERNARD APPEL, Lynn, Mass.
Shamberg's Disease? Presented by DR. ALFRED HOLLANDER, Springfield, Mass.
Majocchi's Disease? Presented by DR. ARTHUR S. SPANGLER, Boston.
Lichen Nitidus. Presented by DR. WILLIAM WOLF, Lowell, Mass.
Psoriasis? Keloids. Presented by DR. LEO KORETSKY, Chelsea, Mass.
Lupus Vulgaris. Presented by DR. H. BERTRAM ULLIAN, Everett, Mass.
Multiple Neurofibromata. Presented by DR. ROBERT H. GOLDFARB, Boston.
Sclerodermatomyositis. Presented by DR. SYDNEY J. ALLMAN, Boston.
Lupus Miliaris Faciei. Presented by DR. WILLIAM J. MACDONALD, Boston.
Toxic Vasculitis. Presented by DR. MAURAY J. TYE, Haverhill, Mass.
Leg Ulcers of Unknown Origin. Presented by DR. MAURAY J. TYE, Haverhill, Mass.
Recurrent Late Cutaneous Syphilis. Presented by DR. WILLIAM R. HILL, Boston.
Chronic Lymphedema, Scleroderma? Raynaud's Disease? Presented by DR. BERNARD APPEL, Lynn, Mass.
Erythema Annulare Centrifugum. Presented by DR. MILDRED L. RYAN, Brockton, Mass.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

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April 1, 1952

Lupus Vulgaris. Presented by DR. SAMUEL IRGANG.

A. P., a boy aged 9, a native of Puerto Rico but a resident of New York City for the past two years, is presented from Harlem Hospital with two coin-sized, sharply marginated, superficial, slightly infiltrated, crusted patches on the anterior and left lateral aspect of the neck. Lymphadenitis (possibly tuberculous) of the left cervical region requiring surgical intervention preceded the development of the lesions by several months.

An x-ray of the chest showed no abnormality of the lungs. An intracutaneous injection of 0.01 cc. of old tuberculin in a dilution of 1:10,000 produced a moderately positive local reaction. Serologic tests of the blood for syphilis were negative. A hemogram was normal except for neutropenia (45%) and lymphocytosis (49%).

Histologic examination showed in the lower half of the cutis foci of miliary epithelioid tubercles with Langhans and foreign body giant cells. Diffuse tuberculoid structure was present in the subpapillary region. The superficial cutis was ulcerated and secondarily infected. Papillomatosis was present. The overlying epidermis was hyperplastic, and crusting was observed on the surface.

Treatment with vitamin D_2 (50,000 units daily) for the past two months has resulted in some improvement.

DISCUSSION

DR. MAURICE J. COSTELLO: These lesions impressed me as being scrofuloderma rather than lupus vulgaris. I have seen typical lesions of lupus vulgaris following tuberculous lymphadenitis, but the crusting, ulceration, and the like seen tonight suggested scrofuloderma, at least, and it more frequently follows lymphadenitis than does lupus vulgaris.

DR. JACK WOLF: I am inclined to agree with the diagnosis of lupus vulgaris. I felt that the lesions were primarily in the skin rather than secondary to the glandular involvement.

DR. PAUL GROSS: It is not necessary to have involvement of the glands in primary scrofuloderma. If this is scrofuloderma, there should be a decided histologic picture; possibly the amount of exudation would be in favor of that diagnosis, but I feel it still might be a case of lupus vulgaris.

DR. NATHAN SOBEL: I don't think that there is any question that it is some form of tuberculosis of the skin, and I would lean toward lupus vulgaris.

DR. WILBERT SACHS: If there were no necrosis in the slide, one would have to accept the diagnosis of lupus vulgaris, but if there is necrosis I don't see how one is going to differentiate between lupus vulgaris and scrofuloderma.

DR. SAMUEL IRGANG: The location of the lesions certainly favors the diagnosis of scrofuloderma, but there is no history of antecedent lymphadenopathy in that location. On palpation we find that the process is superficial. I think that scrofuloderma would show a more extensive necrotic process than is present in this case. I believe that it is lupus vulgaris.

Sporotrichosis. Presented by DR. ROYAL M. MONTGOMERY, for DR. C. DOUGLAS WALSH.

F. S., a man aged 31, was first seen March 3, 1952, because of the presence in the left forearm of four shot-like nodes up to several millimeters in diameter, freely movable subcutaneously. These had been present for several weeks. More recently a tender node had appeared above the elbow. On the dorsal surface of the distal phalangeal joint of the left ring finger was a raised, flat, pink, indurated plaque with a central crust, 1 cm. in diameter. Culture was taken from beneath the crust.

The tuberculin test and the Mazzini reaction of the blood were negative. A roentgenogram of the lungs showed no abnormalities.

Results of the biopsy were reported by Dr. Wilbert Sachs, who found no epidermis present, so that the relationship of the tissue could not be given. However, the entire tissue showed a tremendous cellular reaction. In many places there were numerous epithelioid cells, which appeared to be in tubercle formation. There were also numerous multinucleated giant cells. In other zones, however, there was a pronounced infiltration of small round cells, polymorphonuclear leucocytes, and plasma cells. From the clinical description he felt that sporotrichosis would have to be ruled out. However, the tissue, because of epithelioid cells and more than a suggestion of tubercle formation, did not present the picture one would expect to find in a deep mycosis.

The fingertip received an exposure of 75 r on March 11, and the lesion has partially resolved since then. Administration of potassium iodide was begun on March 25.

The culture was identified as Sporotrichum schenckii.

DISCUSSION

DR. EUGENE T. BERNSTEIN: There were some nodules that looked like Darier-Roussy sarcoid, but some that might fall into the category of sporotrichosis.

DR. ANTHONY C. CIPOLLARO: I don't think anyone can doubt the diagnosis after looking at the cultures, even though they were made from an ulcerated area on one finger, but nodules are certainly unusual features in sporotrichosis. It is a nodular and nonulcerative type.

DR. ROYAL M. MONTGOMERY: Dr. Walsh made the diagnosis. The lesion was apparently superficially ulcerated, and he grew one culture from this and one from the biopsy site on the arm. As Dr. Cipollaro mentioned, it is a nodular nonulcerative type, which is unusual.

Lichen Planus. Presented by DR. SAMUEL IRGANG.

T. M., a Negro aged 49, is presented from Harlem Hospital with a generalized pruritic lichenoid eruption of two and one-half months' duration. It consists of pinhead-sized pinkish-red, shiny papules which have a decided tendency to group and coalesce, forming patches of various sizes. These plaques are brownish and slightly scaly, and some exhibit slight crusting. The patient had taken "666" (a preparation of antipyrine, citric acid, magnesium sulfate, and ammonium chloride), but the eruption developed a week after this medication was discontinued.

Serologic tests of the blood for syphilis were negative. A hemogram showed neutropenia (46%), lymphocytosis (40%), and eosinophilia (6%).

Histologic examination showed the features of lichen planus except for the presence of spongiosis and parakeratosis; the latter layer contained small crusts.

DISCUSSION

DR. EUGENE T. BERNSTEIN: We sometimes see lichen planus in Negroes, but here the picture is unusual. Very often lichen planus closely resembles quinacrine (atabrine®) eruptions. The diagnosis can be established on histological grounds.

DR. LEWIS B. ROBINSON: I have seen more Negroes with lichen planus at the clinic than white people. The lesions are generally larger than those seen in white persons. I would be inclined to think that this was lichen planus.

DR. SAMUEL IRGANG: When we first saw the patient we considered the possibility of drug eruption, but he had stopped taking the medication one week before the eruption occurred, and he has had the eruption for 10 or 11 weeks without signs of resolution. The unusual histologic feature is the parakeratosis and spongiosis. Whether he had at that time a mild form of drug eruption superimposed on lichen planus, I cannot say. I should like to hear what the histologists have to say about that.

DR. WILBERT SACHS: It is quite possible that it started out as a drug eruption and then developed into lichen planus. I have never seen spongiosis or parakeratosis in a full-fledged lichen planus, but I have seen it when it started out as a multiform-erythema-like process that eventuates into lichen planus.

Vitiligo; Response to "Meladinin." Presented by DR. JACK WOLF.

R. H., a woman aged 38, is presented from the Skin and Cancer Unit with vitiligo of six years' duration at the time treatment with "meladinin" (a preparation containing ammoidin and ammidin) was instituted on April 3, 1951. This patient was treated with topical applications of "meladinin" followed by exposure to ultraviolet light in erythema doses. She was unable to tolerate oral medication because of nausea and drowsiness. Altogether, she received little treatment because of her inability to attend the clinic regularly.

At present she shows noticeable return of pigment on the backs of both hands, more pronounced on the left, which received more treatment. In the eight months which have elapsed since the last treatment there has been no regression in the pigmentation which followed treatment.

Vitiligo; Response to "Meladinin." Presented by DR. JACK WOLF.

E. B., a woman aged 40 when first seen on Oct. 7, 1951, gave a history of vitiligo of 30 years' duration. She had been treated with gold, oil of bergamot and ultraviolet radiation, and paraaminobenzoic acid, all without benefit. On Oct. 17, 1951, therapy with "meladinin" paint was begun, followed by exposure to ultraviolet rays. She was also given "meladinin" by mouth, starting with two tablets daily and increasing gradually until a dose of six tablets daily was being taken. The increased dosage produced palpitation and necessitated cessation of treatment temporarily. When resumed several weeks later the medication was tolerated, and there was no reappearance of palpitation even when the six-tablet dose was reached.

After several weeks of treatment pigment began to reappear on the various parts of the body, even in some locations where there was no exposure to ultraviolet rays. The patient was treated approximately once a week until March 3, 1952. While there has not been a complete return of pigment, the improvement has been considerable, with almost complete return of pigment in many locations.

DISCUSSION ON PRECEDING TWO CASES

DR. EUGENE T. BERNSTEIN: In the paper from Cairo some failures and some good results were reported. These two cases are examples of a good result. It is worth while to try this therapy because the disfiguring effect of vitiligo has an unpleasant psychologic result. It is the first time we have had something to cure vitiligo.

DR. KLEIN: One should be careful in judging vitiligo in the winter time and should watch how it behaves in the summer. As it is now, one cannot say anything about the result of this drug.

DR. MAURICE J. COSTELLO: I was not as impressed as Dr. Bernstein. The light was flattering. I think the only thing to do is to make an examination under Wood's light, which gives a decided contrast between the vitiliginous areas and the normal skin. Even on theoretical grounds, it doesn't impress me.

DR. DOUGLAS TORRE: What percentage of the patients under treatment do these two represent?

DR. LOUIS HUTNER (by invitation): Altogether at the Skin and Cancer Clinic we had four cases, and the first two patients did not have large doses of ultraviolet irradiation. The first patient was the only one that stayed with us. The other was a private patient. She came from Louisville, Ky., to be here tonight. As for the toxic effects, the first patient became nauseated after taking two or three tablets and stopped, whereupon the side-effects disappeared immediately. Later she was able to take two tablets but then had to cut it down to one. The other patient took two tablets, got rapid heartbeat when they were increased to six, and later went back to that dosage. It is important to give just an erythema dose of ultraviolet irradiation, according to the Egyptian investigators. Some of their patients went out into the sun, got big blisters, and discontinued treatment.

Sarcoidosis Treated with Cortisone. Presented by DR. LESLIE P. BARKER.

A. M., a Puerto Rican man aged 42, came to St. Luke's Hospital Clinic in 1948 because of multiple painless nodular lesions on the face and left ear of three years' duration. Their development was associated with enlarged glands of the neck and groin and a moderate amount of exertional dyspnea. He had been feeling tired and listless for the same period. There was no history of tuberculosis or other recent disease, but he had had treatment for "bad blood" a few years previously.

Around the mouth, on the left cheek, and on the left ear were several discrete, slightly raised, reddish-brown papules and plaques varying in size from a few millimeters to several centimeters. They were only slightly infiltrated and nontender; slight scaling was present on two lesions. The liver was palpable 3 cm. beneath the right costal margin, and the spleen about 2 cm. The cervical, epitrochlear and inguinal nodes were enlarged, nontender, and freely movable.

A roentgenogram of the chest showed increased hilar adenopathy consistent with sarcoidosis. X-ray examination showed the long bones to be normal. An epitrochlear node and a section of skin from one of the lesions on the face were removed, and both showed typical sarcoid structure histologically. The Kveim test was strongly positive. The blood cell count and urinalyses have been consistently normal. The Mazzini reaction of the blood is consistently 4+ and the Kolmer test negative. Hanger's liver function tests have elicited 3+, 4+, and 2+ reactions. The serum protein has ranged between 7.7 and 8.2 gm. per 100 cc., with the albumin-globulin ratio consistently 4:3, except two weeks ago, when it was 5:3. The erythrocyte sedimentation test has varied from 17 to 44 mm. per hour. The tuberculin test has been consistently negative in a dilution of 1:100.

The patient has been hospitalized eight times for diagnostic procedures and treatment. Summary of treatment: In September, 1948, he was given 0.04 gm. oxophenarsine hydrochloride (mapharsen®) twice weekly for four weeks without effect; in November, 1948, streptomycin (a total of 8.75 gm.) without effect; in January, 1949, vitamin D, 100,000 units daily for one

week (discontinued because of gastrointestinal upset), and in February, 1950, dihydrostreptomycin (a total of 14.5 gm.), with high-vitamin and high-protein diet without improvement.

In December, 1951, administration of cortisone was started, 300 mg. daily for one week, 200 mg. daily for one week, and 100 mg. daily for two weeks. The patient was then discharged from the hospital on a maintenance dosage of 50 mg. daily until March 20, 1952. Four days after the medication was begun the adenopathy had completely disappeared; the cutaneous lesions showed tremendous improvement, almost entirely disappearing within 10 days. There was some recurrence of the cutaneous lesions when the dose of cortisone was reduced to 50 mg., and almost complete recurrence when it was reduced to 25 mg., but they again improved when the dose was increased to 50 mg. daily. Since administration of cortisone was stopped 10 days ago, the patient has complained of some dyspnea on exertion and there has been some recurrence of the cutaneous lesions. Repeated x-rays of the chest have shown no change in the lung involvement.

DISCUSSION

DR. PAUL GROSS: We are dealing with a Puerto Rican, and this doesn't conform to the type of sarcoidosis observed in the Negro population of the United States. I think Dr. Barker has enough evidence to rule out tuberculoid leprosy. The lesions of the ear do resemble lupus vulgaris, and that fits in with the sarcoidosis one sees in Europe and the occasional case observed in the United States.

DR. CARL T. NELSON: I saw that patient approximately three years ago, and he then had much more extensive sarcoid than he shows tonight. The results from cortisone therapy are particularly good in this instance.

DR. NATHAN SOBEL: The health department does not consider the Mazzini reaction as diagnostic but as a screening test, relying much more on the Kolmer. One could not consider syphilis in this case.

DR. S. IRGANG: I don't disagree with the diagnosis, but I have never seen this superficial plaque type of sarcoid in any of my patients. It looks to me like the macular anesthetic type of leprosy. I don't believe leprosy responds to cortisone at all. I have seen sarcoid resolve spontaneously; I have seen it respond to vitamin D_2 and to liver extract. I have not had results with bismuth in the treatment of that disease.

DR. LESLIE P. BARKER: I don't think there is any question about the diagnosis of sarcoid as against leprosy. It shows a typical sarcoid structure histologically. The patient has tremendously enlarged glands and lung involvement; the only thing he doesn't have is bony involvement. He has a number of infiltrated lesions on the cheeks as well as on the ear; within four days of his receiving cortisone many had disappeared, and within a week they had completely disappeared. You wouldn't see that in leprosy.

Stasis and Dystrophic Ulcer in Acrodermatitis Chronica Atrophicans Cured by Ligation of Saphenous Veins.

K. M., a woman aged 65, is presented from St. Luke's Hospital complaining of discoloration and scaling of the right leg, of 15 or 20 years' duration. Three years ago associated varicose veins were ligated because of ulceration on the lower part of the leg. This healed after operation.

Two weeks prior to admission on Sept. 24, 1951, the patient fell and lacerated the anterior aspect of the right knee. The wound failed to heal and enlarged into a superficial granulating ulcer, rectangular in shape, and measuring 10 by 8 cm. There were extensive varicose veins on the same leg. On Sept. 25, 1951, with the patient under local anesthetic, multiple low saphenous ligations were performed on the right leg. The ulcer began to heal rapidly and was finally completely cured.

At present the right leg, from the middle of the thigh to the lower part of the leg, shows a very thin, atrophic, bluish-red, slightly scaly, parchment-like skin which wrinkles easily. There is no evidence of ulceration. Three or four weeks ago a contact type of dermatitis of the arms and legs developed.

DISCUSSION

DR. HELEN O. CURTH: It is an amazing result in anatrophic skin.

DR. MAURICE J. COSTELLO: These patients seldom have real varicosities, and it is difficult for me to understand how this patient got well. Many practitioners inject varicose veins with

sclerosing solutions. The circulation becomes impaired in these skins, and I have seen a number injured by that form of treatment. I am unable to understand how ligating the saphenous vein would help, unless it was the bed rest.

DR. ARTHUR B. HYMAN: The results in healing this ulcer become particularly important because a significant number of cases have been reported of the development of prickle cell epithelioma in acrodermatitis chronica atrophicans. The person facing operation and the one who performed it should be congratulated for preventing the possibility of very serious disease.

DR. LESLIE P. BARKER: The patient definitely had varicose veins in an unusual location, and a large ulcer that wouldn't heal. It did heal after ligation, and the patient had bed rest only for a few days, so I don't think that could account for all of it.

DR. WILLIAM CURTH: Was any examination as to the patency of the deep veins done prior to operation?

DR. ANTHONY C. CIPOLLARO: In connection with Dr. Hyman's remarks regarding the development of cancerous lesions in acrodermatitis chronica atrophicans, some cases have been reported, but my impression is that there are less than 10. George Pack has reported several, and a woman was seen at New York Hospital with extensive carcinoma about the ankle in such a case. The surgeons strongly urged amputation, and it was feared that excision followed by a skin graft would not heal in such skin, but to everyone's surprise the wound did heal beautifully after the plastic operation and the woman still has her leg; metastases have not developed, although it is a year and perhaps more since the operation. In the dermatologic literature there is very little reference to the association of prickle cell epithelioma with acrodermatitis chronica atrophicans.

DR. JUAN LARRALDE: Dr. Costello said that in acrodermatitis chronica atrophicans, varicose veins were only simple dilatations. The effect is the same—stasis in the legs. Operation may have helped the stasis. The patient did not have much rest after the operation.

Acrodermatitis Chronica Atrophicans; Result of Therapy. Presented by DR. ROYAL M. MONTGOMERY.

A. M., a woman aged 50, was previously presented before this society in April, 1951. She first went to the Skin Clinic of the Hospital for Special Surgery in November, 1950, because of an eruption of 18 months' duration which had spread somewhat during the preceding 6 months. The lesions involved the left elbow, forearm, hand, little finger, both knees, and the outer right malleolus, and there were small superficial varices on the lower part of both legs. She was given 300 mg. daily of ephynal® (*d,l*-alpha-tocopherol) acetate without response. Since her previous presentation she has received, during April, May, and June, 1951, a total of 6,600,000 units of penicillin. The redness in all areas gradually diminished. At present there is some erythema over the second and third metacarpophalangeal joints of the left hand, with some atrophy. The skin of the right knee has a pale red color. Some erythema with atrophy is also present over the left knee and left elbow. The induration which was formerly present over the ulna has decreased.

Morphea. Presented by DR. ROYAL M. MONTGOMERY.

Lichen Planus of Scalp Simulating Psoriasis and Lichen Chronicus Simplex. Presented by DR. JOSEPH L. MORSE.

NEW YORK DERMATOLOGICAL SOCIETY

Anthony C. Cipollaro, M.D., *President*

Maurice J. Costello, M.D., *Secretary*

Oct. 23, 1951

A Case for Diagnosis: Seborrheic Dermatitis? Presented by DR. EUGENE F. TRAUB.

E. G. S., a woman aged 59, stated that in November, 1949, a brown spot appeared on her face. She consulted Dr. Parounagian, who treated her in 1932 for syphilis, discovered by a routine blood examination at Woman's Hospital when a fibroid tumor had been removed. Despite local therapy the spot grew larger and at times became red. In August, 1950, she

was seen by Dr. Paul Gross, who prescribed iodochlorhydroxyquin (vioform®) ointment. The eruption cleared temporarily but recurred promptly, and Dr. Gross and Dr. Ellen Reiner diagnosed it as herpes simplex. Aureomycin ointment was given, as the iodochlorhydroxyquin had begun to cause irritation. The patient was then seen by Dr. James W. Anderson, of West Virginia, who diagnosed the eruption as lupus erythematosus and prescribed bismuth sodium triglycollamate ("bistrimate").

The patient was first seen by me, in January, 1951, because of an eruption limited to the face, chiefly the left side. It was erythematous, crusted, and patchy, with some involvement of the eyebrows, nasolabial angles, and general seborrheic areas. The patient was given an x-ray treatment, and a local application of salicylic acid and a sulfonamide compound, and in two or three weeks her skin was practically clear. However, the eruption continued to reappear and finally became uncontrollable on the left side of the face, where a peculiar horseshoe-shaped, serpiginous eruption developed, absolutely characteristic of a late syphilid. At this time all evidence of an eruption resembling seborrhea had disappeared, and, since the patient had had syphilis, it was felt that the present eruption was probably a result of that disease.

Serologic studies made on June 18, 1951, gave the following results: Both the Kolmer and the cardiolipin complement-fixation tests were anticomplementary; the Mazzini test was plus-minus; the Kline exclusion test was negative; both the Rein-Bossak and VDRL cardiolipin reactions were 1+. A course of 10,000,000 units of penicillin was given, with practically no influence on the eruption, and in a second serologic study, on July 16, 1951, the Mazzini test and the Kline exclusion test were negative; the reaction to the VDRL and Rein-Bossak cardiolipin tests was each 1+; the Kolmer-complement-fixation, 2+, and the cardiolipin complement fixation, 4+.

A biopsy specimen examined by Dr. Wilbert Sachs showed the vessels of the mid and upper cutis to be dilated, with pronounced focal and diffuse infiltration of small round cells, wandering connective tissue cells, and an occasional plasma cell. Considerable interstitial edema could be seen throughout the entire cutis. In the upper cutis was pronounced basophilic degeneration. A mild fibroblast cell infiltration could be seen. The epidermis was irregularly acanthotic, and the vessels were dilated and filled with horny plugs. The palisade layer was intact. The surface was covered with a large crust. The elastic tissue was clumped beneath the epidermis. There was no evidence of syphilis or mycosis fungoides. The diagnosis was probable lupus erythematosus.

After cutting further sections at my suggestion, Dr. Sachs made the following report: "The picture still suggests the possibility of lupus erythematosus. However, a possible seborrheic dermatitis or seborrhea congestiva may be considered. A multiform-erythema-like reaction in a skin showing senile changes cannot be entirely ruled out. However, there is no evidence of syphilis or mycosis fungoides."

Large doses of x-rays were given to the large and persistent lesions on the left cheek. Gold was given intravenously, and bismuth sodium triglycollamate was again given internally. Small doses of solid carbon dioxide were applied to the edges of the lesion; this, together with local application of salicylic acid and resorcinol, which appeared to be more satisfactory than any other prescription for local application used to date, temporarily cleared the eruption again.

The patient is presented because various lesions are again appearing and because of the peculiar pattern of the lesions. The histologic report suggesting the possibility of lupus erythematosus does not seem tenable, because the lesions are transient and migrate from one area to another. They are not fixed in discoid patches, as one would expect in lupus erythematosus. At one stage the eruption masqueraded as a syphilid and had every clinical attribute of a late tertiary lesion. In addition to the diagnosis of seborrheic dermatitis, lupus erythematosus, Bowen's disease, syphilis, and even mycosis fungoides have been considered. Apparently the history has excluded most of these.

DISCUSSION

DR. GEORGE M. LEWIS: In a similar patient, I classified the disease as a superficial type of lupus erythematosus without atrophy and without centrifugal characteristics. This is the type of case that worries one, because of the fear that the disease will eventually become the subacute disseminate form. In this benign type, vitamin E may be effective.

DR. GERALD F. MACHACEK: I think it is lupus erythematosus, as Dr. Lewis said.

DR. FRANK C. COMBES: I think there is no doubt that this patient has lupus erythematosus. Down at the lower pole there are four or five small areas which under magnification show typical lupus erythematosus. I can't understand how there can be any question between the extremely superficial lupus erythematosus and tertiary syphilis, which is a deep process in which there is arciform scarring due to serpiginous extension with healing. The nodular syphilid is a deep lesion. I don't see any evidence that the lesions in this patient ever involved the deeper cutis.

DR. EUGENE F. TRAUB: It is obvious that the picture has varied considerably at different times. Good dermatologists have called it lupus erythematosus, herpes recurrens, and tertiary syphilid. The lesions are usually crusted, not scaly, and that has been one of the objections to the diagnosis of lupus erythematosus. Another objection is that the lesions are not fixed but migrate peripherally, healing as they go. This is also against the diagnosis of seborrheic keratosis. It has to be something that is rather ephemeral, and for that reason the diagnosis of seborrheic dermatitis has seemed to fit this peculiar pattern best.

Nevus Comedonicus in Dermatome Distribution. Presented by DR. MAURICE J. COSTELLO.

B. R., a woman aged *63*, is presented with an eruption which has been present since the age of 13. This consists of groups of small, closely aggregated comedones involving the dermatome on the right side corresponding to the third, fourth, fifth, sixth, and seventh cervical nerves. This eruption was noticed on routine examination and is presented because of its rare and bizarre distribution. The patient also has scars of abortive herpes zoster which involved the right second and third lumbar dermatomes.

DISCUSSION

DR. EUGENE F. TRAUB: It is certainly a unilateral nevus. Tonight some of the lesions looked a little warty, and I wonder whether it could be a mixed type of nevus, because I saw few if any comedones. The lesions that came closest to that were enlarged tiny sebaceous plugs. Possibly those that looked verrucous might have represented an area where large groups of comedones had come out. Certainly it is a nevus, and an interesting one.

DR. FRANK C. COMBES: I agree with Dr. Traub; I think it is an incomplete nevus unius lateralis. My interpretation of nevus comedonicus is that it is just hundreds and hundreds of comedones, without this warty appearance.

Sweat Gland Adenoma. Presented by DR. GERALD F. MACHACEK.

M. A., a woman aged *22*, has had a painless flesh-colored tumor on the right heel for nine months. The lesion is *2* by *2* cm., and it developed and grew without producing symptoms until one month ago, when the patient reported to the Vanderbilt Clinic. A diagnosis of plantar wart was made, and the lesion was treated with Phillips' contact x-ray therapy, a dose of 1,500 r being given without response. Biopsy was performed on Sept. *27*, and at the time it was noted that a mucous material was expressed from the cut surface of the lesion.

Histologic examination revealed a thickened epidermis and a hyalinized cutis. Throughout the sections were masses of small cells with large highly chromatic nuclei, which resembled mononuclear leucocytes or epithelial cells and which were found massed around vascular channels and within the blood vessels, as well as invading the fat tissue. A similar picture is seen in certain epithelial tumors arising from sweat glands or their ducts. This is the likely diagnosis in this case. Dr. Stout agreed and advised complete excision of the tumor. The possibility of a glomus tumor was also considered, but the invasion of fat tissue was thought to rule that out.

DISCUSSION

DR. EUGENE F. TRAUB: One would certainly never suspect a lesion of the sweat glands in that location, nor does the clinical appearance suggest that diagnosis. The lesion is rather firm and inflammatory and seems to be invasive. I should like to agree with Dr. Sachs that it must be something of a more malignant nature than just a simple adenoma of the sweat glands.

DR. FRANK C. COMBES: Whatever it is, I think it should be completely excised. I would be interested to know whether it is a basal cell epithelioma arising in a sweat gland. I don't think it would be particularly sensitive to irradiation.

DR. GERALD F. MACHACEK: It did not react to irradiation, and so apparently it was not very sensitive. I tried to indicate in the history that this was a difficult problem, not only clinically but histologically. At first we were inclined, like Dr. Costello, to consider the lesion traumatic, and we were surprised when we saw numerous peculiar cells, which were difficult to classify. Our ultimate decision was that the lesion was a locally progressive tumor, a sweat gland adenoma rather than a carcinoma. I have seen similar tumors which ultimately proved to be cylindromas. We cut numerous sections in this case, and in none did we find changes that would make our decision final. We do feel that it is a locally infiltrating tumor that should be completely removed. It did not have the morphology of a basal cell epithelioma.

Actinomycosis. Presented by DR. GEORGE M. LEWIS.

J. M., a woman aged 21, was previously presented before this society in January, 1950, by the late Dr. A. Benson Cannon.

Six months ago papulopustules and draining sinuses of the outer half of both cheeks developed. This persisted without improvement, in spite of therapy with penicillin, sulfadiazine, and x-rays. Seven weeks ago the patient was given oxytetracycline ("terramycin") and aureomycin, 8 capsules of each daily, plus potassium iodide solution, 90 drops daily. There was reported to have been some improvement in the lesions at the time the patient was first seen by us on Sept. 4. She had had actinomycosis of the cheeks, with positive culture, two years ago, and it was presumed that the present episode represented a recurrence of the infection.

The patient gave a history of sensitivity to penicillin and sulfadiazine, the only evidence being her report that she experienced lightheadedness, weakness, and cramps in the legs after taking these drugs.

Roentgenograms were made of the teeth five to six months ago and of the chest three months ago.

The positive findings were limited to the face. Both cheeks showed deep communicating purulent sinuses, the orifices of which were smooth, reddened, and glazed. No granules were visible.

A direct smear was negative for granules, and culture was negative.

Potassium iodide solution, 90 drops daily, was continued. Because of the rather ill-defined history of penicillin sensitivity, the patient was given penicillin tablets, 50,000 units three times a day. Locally, hot soaks with sulfurate lime solution (Vleminckx's solution), diluted 1:60, were prescribed. The patient showed great improvement within a few days on this regimen. After three days, she was instructed to increase the potassium iodide by one drop daily, the highest amount being 39 drops three times a day. Ten days after therapy was begun, an acneform eruption developed on the face and chest. The patient was instructed to stop using the iodides for two days, and, finally, on Oct. 8 they were discontinued.

At present the original sinus tracts are completely healed, and there is no evidence of actinomycosis. The acneform eruption persists. The patient is still taking penicillin and is using lotio alba locally.

DISCUSSION

DR. J. LOWRY MILLER: After intramuscular injections of penicillin in large doses, the lesions on the right cheek and buttocks cleared up and remained well for about two months; then on the left cheek a small pustule developed, and from that we were never able to obtain Actinomyces. This lesion spread by undermining. From time to time discrete pustules appeared on the shoulders, and from them we did isolate the same type of Actinomyces that we had previously. At no time were granules demonstrated. The reaction to penicillin I think can be interpreted as a reality. Following one of the last intramuscular injections immediate cyanosis developed, due probably to some penicillin in the blood stream. When intramuscular injections were resumed, there was a similar milder reaction. As Dr. Lewis has inferred, this reaction was probably mental, but the patient did put on a beautiful act of imitating the original reaction. Because new lesions were developing in different spots, we thought there was probably a focus of infection, and the most logical place was in the tonsils. We had

planned to wait until after the poliomyelitis season, at which time we were going to give the patient penicillin, aureomycin, and all the other things at one time, and do a tonsillectomy. We put her on temporary therapy to carry her over. At that time the process apparently began to spread rather rapidly, and the lesions became more active. It is certainly an excellent result that we see tonight.

DR. GERALD F. MACHACEK: I examined numerous sections, in none of which did I find any organisms which suggested a diagnosis of actinomycosis. I don't recall whether I did an acid-fast stain. I was led to believe that the patient had nocardiosis, but cultures were presented of Actinomyces. In none of the sections were there any granules, any mycelia, or anything that suggested actinomycosis.

DR. ANTHONY C. CIPOLLARO: When I saw the patient, it was with the background of a proved case of actinomycosis, even though no granules had been found, and I did no further studies. I told her she should see Dr. Lewis. From what I see now, I am inclined to believe that this was simply a pyogenic infection producing these draining sinuses, and the type of therapy carried out by Dr. Lewis was effectual for a pyogenic infection rather than a real actinomycosis. Dr. Lewis has made many cultures and was not able to find the organism. Dr. Cannon made a great many cultures before he was able to isolate the organism. It would seem that these lesions were produced by a common pyogenic organism.

DR. GEORGE M. LEWIS: A year ago, before this society, Dr. Cannon brought cultures and demonstrated them, and everybody agreed that it was proved actinomycosis without granules, which is nocardiosis. During our study of the patient the past few weeks, we saw nothing that looked like an anaerobic or aerobic organism. It was decided to proceed with treatment, since the diagnosis had been made in the past. I would differ with Dr. Cipollaro. It was our impression that the present episode was a recurrence, and I would be perfectly willing to have it go on record as such. It has not been established from where the infection is coming. The tonsils are often incriminated in the ordinary type of actinomycosis, but the organisms may also be found there in normal persons. Should this patient have a tonsillectomy, or should antibiotic therapy be continued for its effect on foci? Dr. Costello pointed out that she tampers with the lesions, and she undoubtedly plays with them most of the time. With so many open areas she is bound to have pyogenic infection. Sulfurated lime solution seemed to be effective, probably against the pyoderma, but it might be tried locally in other patients with actinomycosis.

Case for Diagnosis: Bacteria? Presented by DR. EUGENE F. TRAUB.

Mrs. G. D., a woman aged 31, has a dermatosis involving the hands and feet, of 15 years' duration.

At 15 years of age, at the time of the onset of the menses, a vesiculopustular dermatosis developed on the patient's hands and feet. She has always noted an exacerbation a few days before her menstrual period. At the age of 20 the eruption cleared up after a full course of x-ray treatments and various local medications. She was also free of it during her one pregnancy and for about six months thereafter. She was first seen by me in April, 1950, at which time a clinical diagnosis of dermatophytosis was made, with an id reaction of the hands. Both areas were badly secondarily infected. Three cultures for fungi were negative. In July, 1950, a complete routine series of patch tests, using many articles of the patient's apparel, were all negative.

Between August and November, 1950, treatment consisted of x-ray irradiation, wet dressings, fungicidal agents, and bland ointments, with minimal effect. In November, the first real improvement was noted, from treatment with 5% chrysarobin in chloroform. After a few weeks the patient became sensitized to this drug and it had to be discontinued. In February, 1951, several abscessed teeth were extracted and there was an exacerbation of the eruption, with great improvement a few days later. In May, 1951, tonsillectomy was performed, after which further improvement was shown, only to be followed by another exacerbation associated with an upper respiratory infection. A course of sulfadiazine was instituted without effect. In July, 1951, a mixed Streptococcus and Staphylococcus vaccine was administered in very gradually increasing doses, and this has been continued to the present. A course of oxytetracycline ("terramycin") was instituted in August, 1951, again without effect. Finally,

in September, 1951, the patient was given cortisone, 100 mg. daily, with dramatic improvement in 24 hours. The dose was lowered to 25 mg. daily, and she suffered a mild relapse, and so the dose was increased to 50 mg. daily, and this dose has been maintained to the present.

Blood chemistry studies and urinalyses have always been reported as showing no abnormalities. A pelvic examination showed no abnormalities.

DISCUSSION

DR. FRANK C. COMBES: I agree with the diagnosis. Undoubtedly the patient has a focus of infection somewhere, and the thing to do is isolate the pathogen, prove its pathogenicity, and then go after it in many ways and get rid of it. The patient tells me she has sinus trouble; her tonsils are out, and so her focus of infection may reside in the sinuses. The same organism would probably be found in her large bowel. Efforts should be made to find out what the organism is and go after it with the proper vaccine and whatever antibiotic it is sensitive to.

DR. GEORGE M. LEWIS: I don't believe in the theory of focus of infection to explain pustular psoriasis. I think the cause will be found to be different, as there is not much logic in the concept of bacterid.

DR. PAUL E. BECHET, Elizabeth, N. J.: Dr. Traub's patient shows a tremendous improvement following the use of cortisone. It is interesting to know that this agent might prove of value in pustular bacterid, even though the results may be temporary. In my experience, this dermatosis is extremely obstinate to standard local therapy.

DR. LESLIE P. BARKER: I agree that the diagnosis in this case is probably a bacterid. I think it is interesting that cortisone improved the condition. However, I wonder whether we are justified in using this drug over a long period in a chronic condition that will recur as soon as the drug is stopped.

DR. GERALD F. MACHACEK: It is just as logical to assume that there may be a bacterid as that there may be a trichophytid, tuberculid, etc. It may not be so in actuality, but there is as much logic in this concept.

DR. GEORGE M. LEWIS: That is entirely different. Here you have a recalcitrant pustular sterile eruption that stays for years; in trichophytid the eruption is transient and goes away when the focus is removed. In tuberculid the pathologic findings support the concept.

DR. FRANK E. CORMIA: I agree with Dr. Bechet; this process may improve with cortisone. There have been reports, too, about the successful use of cortisone in so-called pustular bacterid. However, lesions in this patient not only are on the palms and soles but also involve the ankles and wrists. I would classify this condition as primarily a vesicular eruption. I feel that a focus of infection plays no role in this situation. There is a history also of premenstrual exacerbations with, in addition, improvement during pregnancy. I think the patient should be treated with estrogenic hormone during the last half of the menstrual period. I questioned her further, and she stated that the eruption frequently becomes severe without obvious cause. In that case, I think food allergy should be suspected, due to food she takes only occasionally. An elimination diet such as is employed by Flood (Flood, J. M., and Perry, D. J.: Recurrent Vesicular Eruptions of the Hands Due to Food Allergy, *J. Invest. Dermat.* **7**:309, 1946) might be of value.

DR. PAUL E. BECHET: Pustular bacterid is in my opinion a definite entity and can be clinically differentiated from epidermophytosis, but not as easily from pustular psoriasis. From a clinical point of view, I believe that the latter may in future be classed as a variant of bacterid, but it must be admitted that histologically it shows the structure of psoriasis. The differential diagnosis between the two, according to Dr. Andrews, is that pustular bacterid affects adults without any evidence of psoriasis who do have foci of infection in their tonsils, teeth, or sinuses. According to Ormsby and Montgomery, "The abscesses in pustular psoriasis and in a majority if not all, of cases of pustular bacterids are sterile." The same authors state, "We are in agreement with Andrews that much further work needs to be done on this subject." (Andrews, G. C.: Diseases of the Skin, Ed. 3, W. B. Saunders Company, Philadelphia, 1946, p. 262. Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, Ed. 7, Lea & Febiger, Philadelphia, 1948, p. 317.)

DR. ANTHONY C. CIPOLLARO: This is a well-known clinical entity. At one time we give it one name and at other times another. We have no idea what the cause is, with all the work

that has been done. Even though we recognize the process and see it commonly, yet we have not been able to attach a suitable name or give a cause that we agree on. I think both names—bacterid and pustular psoriasis—are bad, but it is an entity, with a poor name and nonagreement as to its cause.

DR. EUGENE F. TRAUB: This case does not exactly fit my concept of pustular bacterid in the accepted sense, and that is why I labeled it simply bacterid. This patient's lesions have seldom been pustular and are not of the character we expect to find in so-called pustular bacterid. Chronic vesicular dermatosis of the hands and feet of unknown origin would perhaps have been a better title. Certainly there is a relationship to infection and a relationship to menstruation and pregnancy. Perhaps we should explore both these angles still further. I think that the striking changes that occur after removal of each of the foci of infection that we uncover are indicative of a relationship. I tried cortisone because, as Dr. Costello says, even temporary relief is highly desirable. The question is what is to be done now. Should we discontinue cortisone and take the chance of having a relapse or should a maintenance dose sufficiently large to keep the patient free of symptoms be continued? We have taken her tonsils and teeth out and made windows in her sinuses. I don't know what else can be done in that direction.

Panniculitis in a Newborn Child of a Diabetic Mother with Adiponecrosis of Breast. Presented by DR. GERALD F. MACHACEK.

D. S., a girl now aged 5 weeks, was delivered normally. She was evidently normal at birth, weighing 3,640 gm. On the sixth day several cutaneous lumps were noticed, which were thought to be cysts. Result of urinalysis was plus-minus. The nodules are still present over the sacral region, the right deltoid, and the left buttock. They vary in size from 0.5 to 2 cm., are movable, elastic but firm, and are situated intracutaneously and subcutaneously. They originally were pale in color but on last inspection were dusky. No obvious tenderness was elicited.

The mother has diabetes, which was discovered in June, 1951, when she was six months pregnant, and she received insulin. In August, 1947, she had undergone a simple mastectomy. Microscopic examination of the excised tumor revealed that it was due to fat necrosis. There is another child, 21 years of age. Between the two pregnancies which resulted in viable offspring, the mother has had five abortions. The serologic examination of the mother for syphilis was negative.

DISCUSSION

DR. EUGENE F. TRAUB: No treatment is indicated, because fat necrosis in the newborn clears up spontaneously.

DR. J. LOWRY MILLER: I agree with the diagnosis of subcutaneous fat necrosis of the newborn. Biopsy, with a study of the chemistry of the fat, will aid in exact diagnosis.

DR. GERALD F. MACHACEK: This case is interesting to me because I was able to observe a group of cases of panniculitis associated with diabetes, which I reported. In going over the literature at that time I found a case of scleroderma neonatorum (adiponecrosis), which also occurred in an infant born of a diabetic mother. I think there is a common factor; it may be that, since many of these cases of panniculitis occur in diabetics or their offspring, this may provide a lead in investigating the question further. In this case the mother also suffered from adiponecrosis of the breast, which is often confused with carcinoma. I have seen a number of diabetic women so affected. This case is more interesting than one of ordinary fat necrosis or panniculitis.

Radiodermatitis and Squamous Cell Epithelioma. Presented by DR. GEORGE M. LEWIS.

B. R., a woman aged 40, had an x-ray epilation of the right side of the scalp 28 years ago, in Lithuania. She states that all the hair and skin were lost from the right side of the scalp after the treatment. The hair has never returned, and one central area of skin never healed. This area continually crusts over, the crust is shed, and another forms. The lesion has spread somewhat in the past two years. Boric acid soaks and various ointments have not helped.

The entire right side of the scalp and the top of the right pinna exhibit atrophy and telangiectasis. This is sharply limited by a straight line across the forehead, ear, and neck and by the curved line at the midscalp. Above the ear is a yellowish, blood-tinged, crusty lesion 3 by 4 cm., with a central depression and one papular lesion 0.5 cm. in diameter.

Biopsy showed a heavy layer of hyperkeratotic crust overlying the epidermis, which in turn showed cyst formation and spongiosis. Many of the cells were undergoing hydropic degeneration. The basal cell layer was intact. The entire dermis was composed of homogenized, degenerated, edematous, collagenous tissue. The blood vessels were somewhat dilated in the few areas where they were present. There was a sparse diffuse infiltration of plasma cells, eosinophiles, and basal inflammatory cells. No malignant cells were seen. The diagnosis is that the condition is compatible with radiodermatitis.

DISCUSSION

DR. EUGENE F. TRAUB: She ought to have a skin graft over that entire scalp area.

DR. GEORGE M. LEWIS: Do you agree with the diagnosis of squamous cell epithelioma?

DR. EUGENE F. TRAUB: Probably, but if one is not already present it will surely develop if the site is not radically removed at once.

DR. PAUL E. BECHET: It might be possible to demonstrate histologic evidence of squamous cell epithelioma by further examination of a number of new serial sections from the same specimen. The late Dr. Frank Fraser reported negative histologic findings in a clinically typical egg-sized carcinoma on the leg of a patient presented by me either before this or the Manhattan Dermatologic Society. On my request, Dr. Fraser kindly examined a dozen or more serial sections from the same block, with positive findings.

DR. ANTHONY C. CIPOLLARO: I agree with Dr. Traub that the patient should have a plastic operation.

DR. FRANK C. COMBES: In cases of postirradiation scarring and atrophy, does the epithelioma arise from the scar tissue, or is it always preceded by a keratosis or ulcer? It has been my observation that a preexisting keratosis, keratoma, or chronic ulcer is always a prerequisite.

DR. GERALD F. MACHACEK: I think you can get any change—angiomas, angioma-like lesions, keratoses, intraepidermal epitheliomas, basal cell epitheliomas, squamous cell epitheliomas, etc. I don't think there must necessarily be a previous keratosis.

DR. ANTHONY C. CIPOLLARO: You can get the epithelioma anywhere. The best evidence is that carcinoma develops in patients with acrodermatitis chronica atrophicans. The ulcer we see in the beginning may be the first evidence of cancer.

DR. EUGENE F. TRAUB: I had a patient with hypertrichosis of the thighs who had been treated with x-rays, and I took a picture showing the radiation sequelae. Three years later she came in with a fungating epithelioma which had developed on what appeared in the original photograph to be relatively slightly damaged skin.

DR. ANTHONY C. CIPOLLARO: Dr. Combes is trying to point out that in radiodermatitis of the superficial type epithelioma doesn't occur. I think that could be dangerous. Any stage of radiodermatitis is fertile soil for epithelioma. We are never justified in producing radiodermatitis with any type of ionizing radiation, including grenz rays and thorium-X.

DR. GEORGE M. LEWIS: In spite of the negative findings, histologically, we believe the lesion is squamous cell epithelioma. There is a possibility of roentgen ulcer.

Melanosis of Undetermined Cause: Lichen Planus? Presented by DR. J. LOWRY MILLER.

I. S., a Jewish woman aged 63, for the past 10 years has noticed tiny red spots within her mouth which would appear like "blood clots" but would soon disappear, leaving only pigmentation at the sites. The lesions were asymptomatic. They occurred on the lips, tongue, and buccal mucosa. In the past few months the patient has noticed dark spots on her neck and chest which were preceded by itching. For the past year there have been changes in the fingernails and toenails consisting of discoloration, thickening, and roughness. This began on the third finger of the right hand, and within a month the remaining fingernails became affected. The toenails became involved subsequently. The patient was seen by a dermatologist, and a diagnosis of nail

dystrophy due to nail polish base was made. Treatment consisted of four x-ray exposures, but this produced no change in the nails. There is no history of drug ingestion. The patient has had three uneventful pregnancies. There have been no previous skin maladies. Two years ago she had a cough and sinusitis, treated with pencillin injections and cough medicine. An x-ray of the chest at that time was normal. It is presumed that the patient has lost 20 lb. (9.1 kg.) during the last two years owing to strict dieting. On the lips and buccal and vaginal mucosae are numerous brown-black, irregular patches showing no activity or atrophy. There is a pigmented patch on the left side of the neck. Between the breasts are a few pigmented, slightly scaly maculopapules. The fingernails and toenails show dystrophic changes with loss of luster, fragmentation, thickening, and brittleness.

Serologic tests for syphilis were negative. Hemoglobin was 14.4 gm. per 100 cc. of blood; there were 7,600 white blood cells, with 65% polymorphonuclear leucocytes and 35% lymphocytes. Results of urinalysis were normal. The serum sodium and chlorides were 142.3 and 107 mEq. per liter, respectively. The plasma carbon-dioxide combining power was 59.8 volumes per 100 cc. Culture from the fingernails showed a nonpathogenic Candida.

DISCUSSION

DR. FRANK C. COMBES: I think this is a case of drug eruption of the lichenoid type with pigmentation. I have never seen this type of melanotic pigmentation following lichen planus, but I have seen it following intake of gold. I think it is typical of the pigmentation seen with gold intoxication. The possibility of absorption from the extensive gold dentures she has worn for 20 years should be considered. If you go over the entire body you can't find lanugo hairs except for two or three on one toe. I think the nail changes and hair loss are also due to gold.

DR. GERALD F. MACHACEK: Only gold—not arsenic?

DR. FRANK C. COMBES: I have never seen that type due to arsenic, but I have seen the "raindrop" type of pigmentation.

DR. EUGENE F. TRAUB: This is the first time I have heard of absorption of gold from a gold filling or inlay, and I wouldn't believe it possible. She may have pigmentation from gold, but not from dentures. You can get mercury dermatitis when amalgam fillings are placed in the teeth, but this occurs only in the process of filling the teeth and not after the metal has been set. There is no later absorption of the mercury nor can there be from the metallic gold.

DR. FRANK E. CORMIA: Didn't Dr. Combes, in a discussion of Dr. Francesco Ronchese's paper, bring out the fact that curving of the nails may follow ingestion of arsenic and/or gold?

DR. J. LOWRY MILLER: Diagnosis is difficult in this case. I put lichen planus down because it was the one possibility to explain the entire picture—the nails, lesions in the mouth, and possibly the pigmentation. We went carefully into the history of drug ingestion, and she is an intelligent patient. The one exception to drugs was a cough medicine given two years ago, and at that time she already had pigmentation of the mouth.

Tuberculid. Presented by DR. GERALD F. MACHACEK.

Leprosy. Presented by DR. GERALD F. MACHACEK.

Secondary Syphilis. Presented by DR. ANTHONY C. CIPOLLARO.

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Radiodermatitis in a Nine-Year-Old Boy. Presented by DR. ANTHONY C. CIPOLLARO.

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Case for Diagnosis: Radiodermatitis, Preexistent, Lupus Erythematosus, Chronic Discoid Type? Presented by DR. ANTHONY C. CIPOLLARO.

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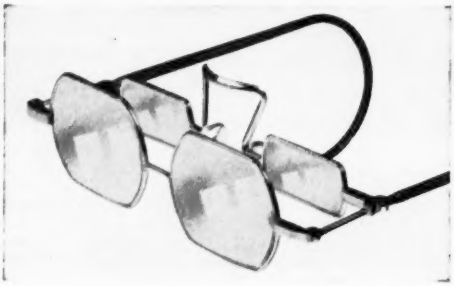

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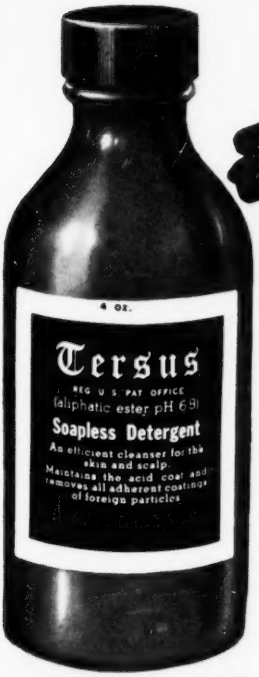
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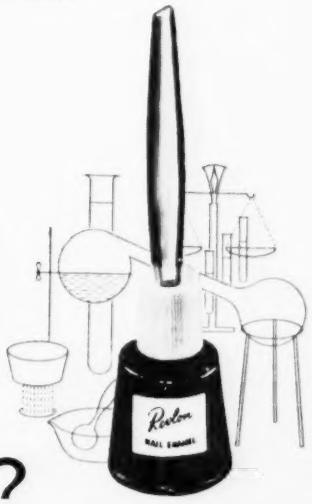

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